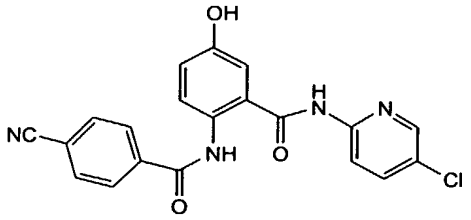
Example 282

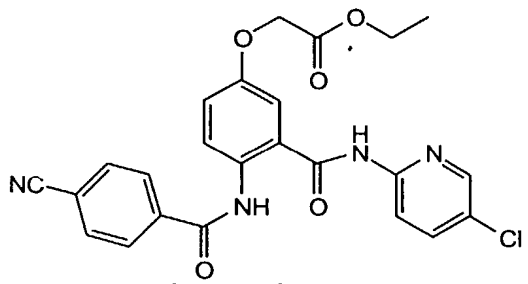
N-(5-chloro(2-pyridyl))\{6-[(4-cyanophenyl)carbonylamino]-3-hydroxyphenyl\}carboxamide



To a suspension of compound N-(5-chloro(2-pyridyl))\{2-[(4-cyanophenyl)-carbonylamino]-5-methoxyphenyl\}carboxamide (500mg, 1.2mmol) in DCM (100mL) at -78°C was added BBr_3 (2mL). The mixture was stirred at ambient temperatures for 72 hours. The solid was collected by filtration and was washed by DCM and water, dried under vacuum. The filtrate was concentrated and extracted with EtOAc. The organic extract was washed with brine, dried and evaporated. The resulting solid was combined with the solid obtained from filtration to give the title compound. Total yield is 90% (430mg). MS found for $C_{20}H_{13}ClN_4O_3$ $(M+H)^+$: 393.0.

Example 283

ethyl 2-\{3-[N-(5-chloro(2-pyridyl))carbamoyl]-4-[(4-cyanophenyl)carbonylamino]-phenoxy\}acetate

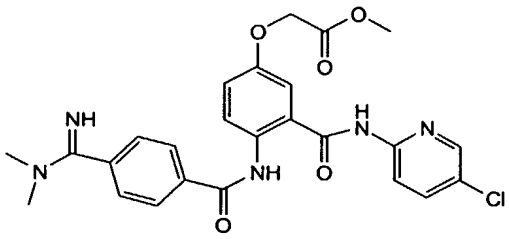


To a mixture of compound N-(5-chloro(2-pyridyl))\{6-[(4-cyanophenyl)-carbonylamino]-3-hydroxyphenyl\}carboxamide (50mg, 0.13mmol) and Cs_2CO_3

(83mg, 0.25mmol) in DMF (1mL) at room temperature was added ethyl bromoacetate (15μL, 0.13mmol). The mixture was stirred for 1 hour before diluted with EtOAc (20mL) and water (10mL). The organic layer was washed with brine dried and evaporated to give 70mg of the crude compound, which was used without farther purification. MS found for $C_{24}H_{19}ClN_4O_5$ $(M+H)^+$: 479.0.

Example 284

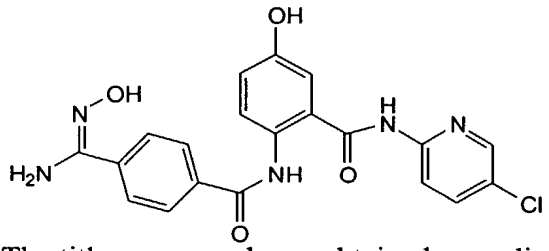
methyl 2-[4-({4-[(dimethylamino)iminomethyl]phenyl}carbonylamino)-3-[N-(5-chloro(2-pyridyl))carbamoyl]phenoxy]acetate



The title compound was obtained according to the procedure described Example 263. MS found for $C_{25}H_{24}ClN_5O_5$ $(M+H)^+$: 510.1.

Example 285

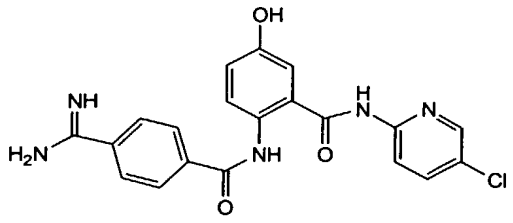
(6-{[4-(amino(hydroxyimino)methyl)phenyl]carbonylamino}-3-hydroxyphenyl)-N-(5-chloro(2-pyridyl))carboxamide



The title compound was obtained according to the procedure described in Example 270. MS found for $C_{20}H_{16}ClN_5O_4$ $(M+Na)^+$: 448.0.

Example 286

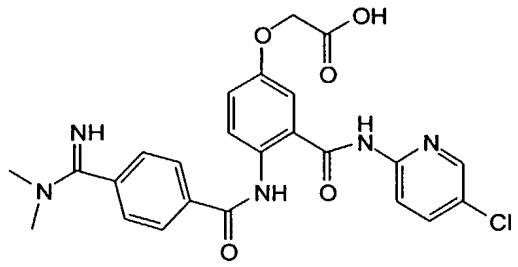
4-(N-{2-[N-(5-chloro(2-pyridyl))carbamoyl]-4-hydroxyphenyl}carbamoyl)-benzenecarboxamidine



The title compound was obtained according to the procedure described in Example 282. MS found for $C_{20}H_{16}ClN_5O_3$ $(M+H)^+$: 410.1.

Example 287

4-(N-{2-[N-(5-chloro(2-pyridyl))carbamoyl]-4-hydroxyphenyl}carbamoyl)-benzenecarboxamidine



To a solution of Example 284 (10mg) in MeOH (1mL) was added 50μL of 1N aq. LiOH solution. The mixture was stirred for 1 hour and purified by RP-HPLC to give the title compound. MS found for $C_{24}H_{22}ClN_5O_5$ $(M+H)^+$: 496.

Without further description, it is believed that one of ordinary skill in the art can, using the preceding description and the illustrative examples, make and utilize the compounds of the present invention and practice the claimed methods. It should be understood that the foregoing discussion and examples merely present a detailed description

of certain preferred embodiments. It will be apparent to those of ordinary skill in the art that various modifications and equivalents can be made without departing from the spirit and scope of the invention. All the patents, journal articles and other documents discussed or cited above are herein incorporated by reference.

WHAT IS CLAIMED IS:

1. A compound of the following formula :

A-Q-D-E-G-J-X

wherein:

A is selected from:

(a) C_1-C_6-alkyl;

(b) C_3-C_8-cycloalkyl;

(c) -N(R^1,R^2), N(R^1,R^2)-C(=NR^3)-, N(R^1,R^2)-C(=NR^3)-N(R^4)-, R^1-C(=NR^3)-, R^1-C(=NR^3)-N(R^4)-;

(d) phenyl, which is independently substituted with 0-2 R substitutuents;

(e) naphthyl, which is independently substituted with 0-2 R substitutuents; and

a monocyclic or fused bicyclic heterocyclic ring system having from 5 to 10 ring atoms, wherein 1-4 ring atoms of the ring system are selected from N, O and S, and wherein the ring system may be substituted with 0-2 R substitutuents;

R is selected from:

H, halo, -CN, -CO_2R^1, -C(=O)-N(R^1, R^2), -$(CH_2)_m$-CO_2R^1, -$(CH_2)_m$-C(=O)-N(R^1, R^2), -NO_2, -SO_2N(R^1, R^2), -SO_2R^1, -$(CH_2)_m$NR^1R^2, -$(CH_2)_m$-C(=NR^3)-R^1, -$(CH_2)_m$-C(=NR^3)-N(R^1,R^2), -$(CH_2)_m$-N(R^4)-C(=NR^3)-N(R^1,R^2), -$(CH_2)_m$NR^1- group appended to a 3 to 6 membered heterocyclic ring containing from 1-4 heteroatoms selected from N, O and S, -C_{1-4}alkyl, -C_{2-6}alkenyl, -C_{2-6}alkynyl, -C_{3-8}cycloalkyl, -C_{0-4}alkylC_{3-8}cycloalkyl, -CF_3, -OR^2, and a 5-6 membered heterocyclic system containing from 1-4 heteroatoms selected from N, O and S, wherein from 1-4 hydrogen atoms on the heterocyclic system may be independently replaced with a member selected from the group consisting of halo, -C_1-C_4-alkyl, -C_{1-4}alkyl-CN, -C_{2-6}alkenyl, -C_{2-6}alkynyl, -C_{3-8}cycloalkyl, -C_{0-4}alkylC_{3-8}cycloalkyl and -NO_2;

m is an integer of 0-2;

R^1, R^2, R^3 and R^4 are independently selected from the group consisting of:
H, $-OR^5$, $-N(-R^5, -R^6)$, $-C_{1-4}$alkyl, $-C_{2-6}$alkenyl, $-C_{2-6}$alkynyl, $-C_{3-8}$cycloalkyl, $-C_{0-4}$alkylC_{3-8}cycloalkyl, $-C_{0-4}$alkylphenyl and $-C_{0-4}$alkylnaphthyl, wherein from 1-4 hydrogen atoms on the ring atoms of the phenyl and naphthyl moieties may be independently replaced with a member selected from the group consisting of halo, $-C_{1-4}$alkyl, $-C_{2-6}$alkenyl, $-C_{2-6}$alkynyl, $-C_{3-8}$cycloalkyl, $-C_{0-4}$alkylC_{3-8}cycloalkyl, -CN, and $-NO_2$; or

R^1 and R^2, or R^2 and R^3 taken together can form a 3-8 membered cycloalkyl or a heterocyclic ring system, wherein the heterocyclic ring system may have from 3 to 10 ring atoms, with 1 to 2 rings being in the ring system and contain from 1-4 heteroatoms selected from N, O and S, wherein from 1-4 hydrogen atoms on the heterocyclic ring system may be independently replaced with a member selected from the group consisting of halo, C_1-C_4-alkyl, -CN $-C_{1-4}$alkyl, $-C_{2-6}$alkenyl, $-C_{2-6}$alkynyl, $-C_{3-8}$cycloalkyl, $-C_{0-4}$alkylC_{3-8}cycloalkyl and $-NO_2$;

R^5 and R^6 are independently selected from the group consisting of:
H, $-C_{1-4}$alkyl, $-C_{2-6}$alkenyl, $-C_{2-6}$alkynyl, $-C_{3-8}$cycloalkyl, $-C_{0-4}$alkylC_{3-8}cycloalkyl, $-C_{0-4}$alkylphenyl and $-C_{0-4}$alkylnaphthyl, wherein from 1-4 hydrogen atoms on the ring atoms of the phenyl and naphthyl moieties may be independently replaced with a member selected from the group consisting of halo, $-C_{1-4}$alkyl, $-C_{2-6}$alkenyl, $-C_{2-6}$alkynyl, $-C_{3-8}$cycloalkyl, $-C_{0-4}$alkylC_{3-8}cycloalkyl, -CN, and $-NO_2$; or

R^5 and R^6 taken together can form a 3-8 membered cycloalkyl or a heterocyclic ring system, wherein the heterocyclic ring system may have from 3 to 10 ring atoms, with 1 to 2 rings being in the ring system and contain from 1-4 heteroatoms selected from N, O and S, wherein from 1-4 hydrogen atoms on the heterocyclic ring system may be independently replaced with a member selected from the group consisting of halo, $-C_1$-C_4-alkyl, -CN $-C_{1-4}$alkyl, $-C_{2-6}$alkenyl, $-C_{2-6}$alkynyl, $-C_{3-8}$cycloalkyl, $-C_{0-4}$alkylC_{3-8}cycloalkyl and $-NO_2$;

Q is a member selected from the group consisting of:

a direct link, -CH_2-, -C(=O)-, -O-, -N(R^7)-, -N(R^7)CH_2-, - CH_2N(R^7) -, -C(=NR^7)-, -C(=O)-N(R^7)-, -N(R^7)-C(=O)-, -S-, -SO-, -SO_2-, -SO_2-N(R^7)- and –N(R^7)-SO_2-;

R^7 is selected from:

H, -C_{1-4}alkyl, -C_{2-6}alkenyl, -C_{2-6}alkynyl, -C_{3-8}cycloalkyl, -C_{0-4}alkylC_{3-8}cycloalkyl, -C_{0-4}alkylphenyl and -C_{0-4}alkylnaphthyl, wherein from 1-4 hydrogen atoms on the ring atoms of the phenyl and naphthyl moieties may be independently replaced with a member selected from the group consisting of halo, -C_{1-4}alkyl, -C_{2-6}alkenyl, -C_{2-6}alkynyl, -C_{3-8}cycloalkyl, -C_{0-4}alkylC_{3-8}cycloalkyl, -CN, and -NO_2;

D is a direct link or is a member selected from the group consisting of:

(a) phenyl, which is independently substituted with 0-2 R^{1a} substitutuents;

(b) naphthyl, which is independently substituted with 0-2 R^{1a} substitutuents; and

(c) a monocyclic or fused bicyclic heterocyclic ring system having from 5 to 10 ring atoms, wherein 1-4 ring atoms of the ring system are selected from N, O and S, and wherein the ring system may be subsituted from 0-2 R^{1a} substitutuents;

R^{1a} is selected from:

halo, -C_{1-4}alkyl, -C_{2-6}alkenyl, -C_{2-6}alkynyl, -C_{3-8}cycloalkyl, -C_{0-4}alkylC_{3-8}cycloalkyl, -CN, -NO_2, -$(CH_2)_n NR^{2a}R^{3a}$, -$(CH_2)_n CO_2R^{2a}$, -$(CH_2)_n CONR^{2a}R^{3a}$, -$SO_2NR^{2a}R^{3a}$, -SO_2R^{2a}, -CF_3, -OR^{2a}, and a 5-6 membered aromatic heterocyclic system containing from 1-4 heteroatoms selected from N, O and S, wherein from 1-4 hydrogen atoms on the aromatic heterocyclic system may be independently replaced with a member selected from the group consisting of halo, -C_{1-4}alkyl, -C_{2-6}alkenyl, -C_{2-6}alkynyl, -C_{3-8}cycloalkyl, -C_{0-4}alkylC_{3-8}cycloalkyl, -CN and -NO_2;

R^{2a} and R^{3a} are independently selected from the group consisting of:

H, -C_{1-4}alkyl, -C_{2-6}alkenyl, -C_{2-6}alkynyl, -C_{3-8}cycloalkyl, -C_{0-4}alkylC_{3-8}cycloalkyl, -C_{0-4}alkylphenyl and -C_{0-4}alkylnaphthyl, wherein from 1-4 hydrogen atoms on the ring atoms of the phenyl and naphthyl moieties may be

independently replaced with a member selected from the group consisting of halo, -C_{1-4}alkyl, -C_{2-6}alkenyl, -C_{2-6}alkynyl, -C_{3-8}cycloalkyl, -C_{0-4}alkylC_{3-8}cycloalkyl, -CN and -NO_2;

n is an integer of 0-2;

E is a direct link or a member selected from the group consisting of: -C_{1-2}-alkyl-, -O-, -S-, -SO-, -SO_2-, -C_{0-1}-alkyl-C(=O), -C_{0-1}-alkyl-C(=O)-N(-R^8)-C_{0-1}-alkyl-, -C_{0-1}-alkyl-N(-R^8)-C(=O)-C_{0-1}-alkyl-, -N(-R^8)-C(=O)-N(-R^8)- and -C_{0-1}-alkyl-N(-R^8)-;

R^8 is a member selected from the group consisting of: H; -C_{1-4}-alkyl; -C_{0-4}-alkylaryl; -C_{0-4}-alkyl-heteroaryl; -C_{1-4}-alkyl-C(=O)-OH, -C_{1-4}-alkyl-C(=O)-O-C_{1-4}-alkyl, and -C_{1-4}-alkyl-C(=O)-N(-R^{2b}, -R^{3b});

R^{2b} and R^{3b} are each a member independently selected from the group consisting of: H, -C_{1-4}-alkyl, -C_{0-4}-alkyl-aryl; -C_{0-4}-alkyl-heterocyclic group, and R^{2b} and R^{3b} together with the N atom to which they are attached can form a 5-8 membered heterocyclic ring containing 1-4 heteroatoms selected from N, O and S, wherein the heterocyclic ring may be substituted with 0-2 R^{1c} groups;

R^{1c} is a member selected from the group consisting of: Halo; -C_{1-4}-alkyl; -CN, -NO_2; -C(=O)-N(-R^{2c}, -R^{3c}); -C(=O)-OR^{2c}; -$(CH_2)_q$-N(-R^{2c}, -R^{3c}); -SO_2-N(-R^{2c}, -R^{3c}); -SO_2R^{2c}; -CF_3 and -$(CH_2)_q$-OR^{2c};

R^{2c} and R^{3c} are each independently a member selected from the group consisting of: H; -C_{1-4}-alkyl and -C_{1-4}-alkyl-aryl;

q is an integer of 0-2;

G is a member selected from the group consisting of:

(a) C_2-alkenyl or C_{3-8}-cycloalkenyl, wherein the alkenyl and cycloalkenyl attachment points are the alkenyl carbon atoms and wherein the -C_2-alkenyl or -C_{3-8}-cycloalkenyl are substituted with 0-4 R^{1d} groups;

(b) a phenylene group wherein the ring carbon atoms of the phenylene group are substituted with 0-4 R^{1d} groups;

(c) a 3-8 membered a saturated, partially unsaturated or aromatic monocyclic- heterocyclic ring system containing 1-4 heteroatoms selected from N, O and S, wherein 0-2 ring atoms of the heterocyclic ring may be substituted with 0-4 R^{1d} groups; and,

(d) an 8-10 membered fused heterocyclic bicyclic ring system, containing 1-4 heteroatoms selected from N, O and S, wherein 0-2 ring atoms of the fused bicyclic ring system may be substituted with 0-4 R^{1d} groups;

R^{1d} is a member selected from the group consisting of:

H, halo; C_{1-6}-alkyl, carbocylic aryl, -CN; $-NO_2$; $-(CH_2)_{0-6}-NR^{2d}R^{3d}$; $-SO_2NR^{2d}R^{3d}$; $-SO_2R^{2d}$; $-CF_3$; $-(CH_2)_{0-6}-OR^{2d}$; $-O-(CH_2)_{1-6}OR^{2d}$; $-O-(CH_2)_{1-6}-C(=O)-O-R^{2d}$; $-O-(CH_2)_{1-6}-C(=O)-N(R^{2d},R^{3d})$; $-N(R^{5a})-(CH_2)_{1-6}-OR^{2d}$; $-N(R^{5a})-(CH_2)_{1-6}-N(R^{2d},R^{3d})$; $-C(=O)-N(R^{2d},R^{3d})$; $-N(R^{5a})-(CH_2)_{1-6}-C(=O)-N(R^{2d},R^{3d})$; $-N(-(CH_2)_{1-6}-OR^{2d})_2$; $-N(R^{5a})-(CH_2)_{1-6}-OR^{2d}$; $-N(R^{5a})-C(=O)-R^{2d}$; $-N(R^{5a})-SO_2-R^{2d}$; $-(CH_2)_{0-6}-C(=O)-O-R^{2d}$; $-(CH_2)_{0-6}-C(=O)-N(R^{2d},R^{3d})$; $-(CH_2)_{0-6}-C(=NR^{2d})-N(R^{3d},R^{4d})$; $-(CH_2)_{0-6}-N(R^{5a})C(=NR^{2d})-N(R^{3d},R^{4d})$; a $-(CH_2)_{0-6}-N(R^{3d})C_{5-6}$ membered saturated, partially unsaturated or aromatic heterocyclic ring containing 1-4 heteroatoms selected from N, O and S, and a $-(CH_2)_{0-6}$-5-6 membered saturated, partially unsaturated or aromatic heterocyclic ring containing 1-4 heteroatoms selected from N, O and S;

R^{5a}, R^{2d}, R^{3d} and R^{4d} are each independently a member selected from the group consisting of:

H, C_{1-6}-alkyl and C_{1-6}-alkylaryl, -CN; $-NO_2$; carbocylic aryl, -CN; $-NO_2$; or

R^{2d} and R^{3d} taken together with the N atoms they are independently attached form a 5-7 membered saturated, partially unsaturated or aromatic heterocyclic ring; or

R^{3d} and R^{4d} taken together with the N atom to which they are attached form a 5-8 membered saturated, partially unsaturated or aromatic heterocyclic ring containing 1-4 heteroatoms selected from N, O and S;

J is a direct link or is a member selected from the group consisting of:
$-N(-R^9)-C(=O)-$; $-C(=O)-N(-R^9)-$; $-O-$; $-S-$; $-SO-$; $-SO_2-$; $-CH_2-$; $-N(-R^9)-$; and $-N(-R^9)-SO_2-$;

R^9 is a member selected from the group consisting of:
H; $-C_{1-4}$-alkyl; $-C_{0-4}$-alkyl-carbocyclic aryl; $-(CH_2)_{0-4}$-5-6 membered saturated, partially unsaturated or aromatic heterocyclic ring containing 1-4 heteroatoms selected from N, O and S; $-(CH_2)_{1-6}-C(=O)-O-C_{1-4}$-alkyl; and $-(CH_2)_{1-6}-C(=O)-N(R^{6a},R^{6b})$;

R^{6a} and R^{6b} are each a member independently selected from the group consisting of:
H and $-C_{1-6}$-alkyl;

X is a member selected from the group consisting of:

(a) phenyl substituted with 0-3 R^{1e} groups;

(b) naphthyl substituted with 0-3 R^{1e} groups and

(c) a 6-membered aromatic heterocyclic ring system containing 1-3 N atoms and having 0-3 ring atoms substituted with 0-3 R^{1e} groups; and

(d) an 8-10 membered fused aromatic heterocyclic bicyclic ring system containing 1-4 heteroatoms selected from N, O and S and 0-3 ring atoms of the fused heterocyclic bicyclic ring system are substituted with 0-3 R^{1e} groups;

R^{1e} is a member independently selected from the group consisting of:
Halo; CF_3; $-C_{1-4}$-alkyl; carbocyclic aryl; $-C_{0-2}$-alkyl-CN; $-O-R^{2e}$; $-C_{0-2}$-alkyl-$C(=O)-O-R^{2e}$; $-C_{0-2}$- alkyl-$C(=O)-N(R^{2e}, R^{3e})$; $-C_{0-2}$-alkyl-NO_2; $-C_{0-2}$-alkyl-$N(R^{2e}, R^{3e})$; $-C_{0-2}$-alkyl-$SO_2-N(R^{2e}, R^{3e})$; $-C_{0-2}$-alkyl-SO_2-R^{2e}; trihaloalkyl; $-O-C_{0-2}$-alkyl-$O-R^{2e}$; $-C_{0-2}$-alkyl-$O-R^{2e}$; $-O-C_{1-4}$-alkyl-

$C(=O)$-$N(R^{2e}, R^{3e})$; -O-C_{1-4}-alkyl-$C(=O)$-O-R^{2e}; -C_{0-2}-alkyl-$N(R^{2e})$-$C(=O)$-R^{3e}; -C_{0-2}-alkyl-$N(-R^{2e})$-SO_2-R^{3e}; -CH_2-$N(R^{2e})$-$C(=O)$-R^{3e} ;-CH_2-$N(R^{2e})$-SO_2-R^{3e}; -$(CH_2)_{0-6}$-$NR^{2e}R^{3e}$; -$C(=O)$-$N(R^{2e},R^{3e})$; -$N(-(CH_2)_{1-6}$-$OR^{2e})_2$; -$N(R^{10})$-$(CH_2)_{1-6}$-OR^{2e}; -$N(R^{10})$-$C(=O)$-R^{2e}; -$N(R^{10})$-SO_2-R^{2e}; -$C(=N(R^{10}))$-$N(R^{2e},R^{3e})$; and a -$(CH_2)_{0-6}$-5-6 membered saturated, partially unsaturated or aromatic heterocyclic ring containing 1-4 heteroatoms selected from N, O and S;

R^{10}, R^{2e} and R^{3e} are each independently a member selected from the group consisting of:

H; -C_{1-4}-alkyl; -C_{0-2}-alkyl-O-R^{1g}; -C_{0-2}-alkyl-$N(-R^{1g}, -R^{2g})$;-C_{1-4}-alkyl-carbocyclic aryl; -C_{1-4}-alkyl-heterocyclic; and R^{10} and R^{2e}, or R^{2e} and R^{3e} together with the N atom to which they are attached can form 5-8 membered heterocyclic ring containing 1-4 heteroatoms selected from N, O and S which can be substituted with 0-2 R^{1g} groups;

R^{1g} and R^{2g} are indepedently a member selected from the group of:

H; halo; -C_{1-4}-alkyl, a carbocyclic aryl group ; a saturated, partially unsaturated or aromatic heterocyclic group; -CN; -$C(=O)$-$N(R^{3g})R^{4g}$; -$C(=O)$-OR^{3g}; -NO_2; -$(CH_2)_p$-$NR^{3g}R^{4g}$; -$SO_2NR^{3g}R^{4g}$; -SO_2R^{3g}; -CF_3; and -$(CH_2)_pOR^{3g}$;

p is an integer of 0-2;

R^{3g} and R^{4g} are each independently selected from the group consisting of:

H; C_{1-4}-alkyl and -C_{0-4}-alkyl-carbocyclic aryl;

and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.

2. A compound of claim 1, wherein:

A is selected from:

(a) C_1-C_6-alkyl;

(b) C_3-C_8-cycloalkyl;

(c) -N(R^1,R^2), N(R^1,R^2)-C(=NR^3)-, N(R^1,R^2)-C(=NR^3)-N(R^4)-, R^1-C(=NR^3)-, R^1-C(=NR^3)-N(R^4)-;

(d) phenyl, which is independently substituted with 0-2 R substitutuents;

(e) naphthyl, which is independently substituted with 0-2 R substitutuents; and

(f) monocyclic or fused bicyclic heterocyclic ring system having from 5 to 10 ring atoms, wherein 1-4 ring atoms of the ring system are selected from N, O and S, and wherein the ring system may be substituted with 0-2 R substitutuents;

R is selected from:

H, halo, -CN, -CO_2R^1, -C(=O)-N(R^1, R^2), -$(CH_2)_m$-CO_2R^1, -$(CH_2)_m$-C(=O)-N(R^1, R^2), -NO_2, -SO_2N(R^1, R^2), -SO_2R^1, -$(CH_2)_m$NR^1R^2, -$(CH_2)_m$-C(=NR^3)-R^1, -$(CH_2)_m$-C(=NR^3)-N(R^1,R^2), -$(CH_2)_m$-N(R^4)-C(=NR^3)-N(R^1,R^2), -$(CH_2)_m$NR^1- group attached to a 3-6 membered heterocylic ring having from 1 to 3 heteroatoms selected from the group consisting of N, O and S, -C_{1-4}alkyl, -C_{2-6}alkenyl, -C_{2-6}alkynyl, -C_{3-8}cycloalkyl, -C_{0-4}alkylC_{3-8}cycloalkyl, -CF_3, -OR^2, and a 5-6 membered heterocyclic aromatic or partially saturated system, including imidazoline, containing from 1-4 heteroatoms selected from N, O and S, wherein from 1-4 hydrogen atoms on the heterocyclic system may be independently replaced with a member selected from the group consisting of halo, -methyl, -C_2-C_4-alkyl, -CN, -C_{2-6}alkenyl, -C_{2-6}alkynyl, -C_{3-8}cycloalkyl, -C_{0-4}alkylC_{3-8}cycloalkyl and -NO_2;

m is an integer of 0-2;

R^1, R^2, R^3 and R^4 are independently selected from the group consisting of:

H, -OR^5, -N(-R^5, -R^6), -C_{1-4}alkyl, -C_{2-6}alkenyl, -C_{2-6}alkynyl, -C_{3-8}cycloalkyl, -C_{0-4}alkylC_{3-8}cycloalkyl, -C_{0-4}alkylphenyl and -C_{0-4}alkylnaphthyl, wherein from 1-4 hydrogen atoms on the ring atoms of the phenyl and naphthyl moieties may be independently replaced with a member selected from the group

consisting of halo, -C_{1-4}alkyl, -C_{2-6}alkenyl, -C_{2-6}alkynyl, -C_{3-8}cycloalkyl, -C_{0-4}alkylC_{3-8}cycloalkyl, -CN, and -NO_2; or

R^1 and R^2, or R^2 and R^3 taken together can form a 3-8 membered cycloalkyl or a heterocyclic ring system, wherein the heterocyclic ring system may have from 3 to 10 ring atoms, with 1 to 2 rings being in the ring system and contain from 1-4 heteroatoms selected from N, O and S, wherein from 1-4 hydrogen atoms on the heterocyclic ring system may be independently replaced with a member selected from the group consisting of halo, C_1-C_4-alkyl, -CN -C_{1-4}alkyl, -C_{2-6}alkenyl, -C_{2-6}alkynyl, -C_{3-8}cycloalkyl, -C_{0-4}alkylC_{3-8}cycloalkyl and -NO_2;

R^5 and R^6 are independently selected from the group consisting of:

H, -C_{1-4}alkyl, -C_{2-6}alkenyl, -C_{2-6}alkynyl, -C_{3-8}cycloalkyl, -C_{0-4}alkylC_{3-8}cycloalkyl, -C_{0-4}alkylphenyl and -C_{0-4}alkylnaphthyl, wherein from 1-4 hydrogen atoms on the ring atoms of the phenyl and naphthyl moieties may be independently replaced with a member selected from the group consisting of halo, -C_{1-4}alkyl, -C_{2-6}alkenyl, -C_{2-6}alkynyl, -C_{3-8}cycloalkyl, -C_{0-4}alkylC_{3-8}cycloalkyl, -CN, and -NO_2; or

R^5 and R^6 taken together can form a 3-8 membered cycloalkyl or a heterocyclic ring system, wherein the heterocyclic ring system may have from 3 to 10 ring atoms, with 1 to 2 rings being in the ring system and contain from 1-4 heteroatoms selected from N, O and S, wherein from 1-4 hydrogen atoms on the heterocyclic ring system may be independently replaced with a member selected from the group consisting of halo, C_1-C_4-alkyl, -CN -C_{1-4}alkyl, -C_{2-6}alkenyl, -C_{2-6}alkynyl, -C_{3-8}cycloalkyl, -C_{0-4}alkylC_{3-8}cycloalkyl and -NO_2;

Q is a member selected from the group consisting of:

a direct link, -CH_2-, -C(=O)-, -O-, -NH-, -NMe-, -$NHCH_2$-, -$NMeCH_2$-, -CH_2NH-, -C(=NH)-, -C(=O)-NH-, -NH-C(=O)-, -CH_2NMe-, -C(=NMe)-;

D is a direct link or is a member selected from the group consisting of:

(a) phenyl, which is independently substituted with 0-2 R^{1a} substitutuents;

(b) naphthyl, which is independently substituted with 0-2 R^{1a} substitutuents; and

a monocyclic or fused bicyclic heterocyclic ring system having from 5 to 10 ring atoms, wherein 1-4 ring atoms of the ring system are selected from N, O and S, and wherein the ring system may be subsituted from 0-2 R^{1a} substitutuents;

R^{1a} is selected from:

halo, -C_{1-4}alkyl, -C_{2-6}alkenyl, -C_{2-6}alkynyl, -C_{3-8}cycloalkyl, -C_{0-4}alkylC_{3-8}cycloalkyl, -CN, -NO_2, -$(CH_2)_nNR^{2a}R^{3a}$, -$(CH_2)_nCO_2R^{2a}$, -$(CH_2)_nCONR^{2a}R^{3a}$, -$SO_2NR^{2a}R^{3a}$, -SO_2R^{2a}, -CF_3, -OR^{2a}, and a 5-6 membered aromatic heterocyclic system containing from 1-4 heteroatoms selected from N, O and S, wherein from 1-4 hydrogen atoms on the aromatic heterocyclic system may be independently replaced with a member selected from the group consisting of halo, -C_{1-4}alkyl, -C_{2-6}alkenyl, -C_{2-6}alkynyl, -C_{3-8}cycloalkyl, -C_{0-4}alkylC_{3-8}cycloalkyl, -CN and -NO_2;

R^{2a} and R^{3a} are independently selected from the group consisting of:

H, -C_{1-4}alkyl, -C_{2-6}alkenyl, -C_{2-6}alkynyl, -C_{3-8}cycloalkyl, -C_{0-4}alkylC_{3-8}cycloalkyl, -C_{0-4}alkylphenyl and -C_{0-4}alkylnaphthyl, wherein from 1-4 hydrogen atoms on the ring atoms of the phenyl and naphthyl moieties may be independently replaced with a member selected from the group consisting of halo, -C_{1-4}alkyl, -C_{2-6}alkenyl, -C_{2-6}alkynyl, -C_{3-8}cycloalkyl, -C_{0-4}alkylC_{3-8}cycloalkyl, -CN and -NO_2;

n is an integer of 0-2;

E is a member selected from the group consisting of:

a direct link, -O-, -NH-, -CH_2NH-, -NHCH_2-, -NMe-, -NH-C(=O)-NH-, -C(=O)-NH-, -NH-C(=O)-;

G is a member selected from the group consisting of:

(a) a C_2-alkenyl group or a C_{3-8}-cycloalkenyl group, wherein the alkenyl group and cycloalkenyl group attachment points are the alkenyl carbon

atoms and wherein the C_2-alkenyl group or C_{3-8}-cycloalkenyl group is substituted with 0-4 R^{1d} groups;

(b) a phenylene group wherein the ring carbon atoms of the phenylene group are substituted with 0-4 R^{1d} groups;

(c) a 3-8 membered a saturated, partially unsaturated or aromatic monocyclic- heterocyclic ring system containing 1-4 heteroatoms selected from N, O and S, wherein 0-4 ring atoms of the heterocyclic ring may be substituted with 0-4 R^{1d} groups; and,

(d) an 8-10 membered fused heterocyclic bicyclic ring system, containing 1-4 heteroatoms selected from N, O and S, wherein 0-4 ring atoms of the fused bicyclic ring system may be substituted with 0-4 R^{1d} groups;

R^{1d} is a member selected from the group consisting of:

H, halo; C_{1-6}-alkyl, carbocylic aryl, -CN; $-NO_2$; $-(CH_2)_{0-6}-NR^{2d}R^{3d}$; $-SO_2NR^{2d}R^{3d}$; $-SO_2R^{2d}$; $-CF_3$; $-(CH_2)_{0-6}-OR^{2d}$; $-O-(CH_2)_{1-6}OR^{2d}$; $-O-(CH_2)_{1-6}-C(=O)-O-R^{2d}$; $-O-(CH_2)_{1-6}-C(=O)-N(R^{2d},R^{3d})$; $-N(R^{5a})-(CH_2)_{1-6}-OR^{2d}$; $-N(R^{5a})-(CH_2)_{1-6}-N(R^{2d},R^{3d})$; $-C(=O)-N(R^{2d},R^{3d})$; $-N(R^{5a})-(CH_2)_{1-6}-C(=O)-N(R^{2d},R^{3d})$; $-N(-(CH_2)_{1-6}-OR^{2d})_2$; $-N(R^{5a})-(CH_2)_{1-6}-OR^{2d}$; $-N(R^{5a})-C(=O)-R^{2d}$; $-N(R^{5a})-SO_2-R^{2d}$; $-(CH_2)_{0-6}-C(=O)-O-R^{2d}$; $-(CH_2)_{0-6}-C(=O)-N(R^{2d},R^{3d})$; $-(CH_2)_{0-6}-C(=NR^{2d})-N(R^{3d},R^{4d})$; $-(CH_2)_{0-6}-N(R^{5a})C(=NR^{2d})-N(R^{3d},R^{4d})$; and a $-(CH_2)_{0-6}-N(R^{3d})$ group wich is attached via the nitrogen atom to a carbon atom of a 5 to 6 membered saturated, partially unsaturated or aromatic heterocyclic ring containing 1-4 heteroatoms selected from N, O and S, and a $-(CH_2)_{0-6}-$ group attached to a 5-6 membered saturated, partially unsaturated or aromatic heterocyclic ring containing 1-4 heteroatoms selected from N, O and S;

R^{5a}, R^{2d}, R^{3d} and R^{4d} are each independently a member selected from the group consisting of:

H, C_{1-6}-alkyl and C_{1-6}-alkylaryl, -CN; $-NO_2$; carbocylic aryl, -CN; $-NO_2$; or

R^{2d} and R^{3d} taken together with the N atoms ther are independently attached form a 5-7 membered saturated, partially unsaturated or aromatic heterocyclic ring; or

R^{3d} and R^{4d} taken together with the N atom to which they are attached form a 5-8 membered saturated, partially unsaturated or aromatic heterocyclic ring containing 1-4 heteroatoms selected from N, O and S;

J is a member selected from the group consisting of:
a direct link, -O-, -NH-, -NMe-, -C(=O)-NH-, -NH-C(=O)-;

X is a member selected from the group consisting of:

(a) phenyl substituted with 0-3 R^{1e} groups;

(b) naphthyl substituted with 0-3 R^{1e} groups and

(c) a 6-membered aromatic heterocyclic ring system containing 1-3 N atoms and having 0-3 ring atoms substituted with 0-3 R^{1e} groups; and

(d) an 8-10 membered fused aromatic heterocyclic bicyclic ring system containing 1-4 heteroatoms selected from N, O and S and 0-3 ring atoms of the fused heterocyclic bicyclic ring system are substituted with 0-3 R^{1e} groups;

R^{1e} is a member independently selected from the group consisting of:
Halo; CF_3; $-C_{1-4}$-alkyl; carbocyclic aryl; $-C_{0-2}$-alkyl-CN; $-O-R^{2e}$; $-C_{0-2}$-alkyl-$C(=O)-O-R^{2e}$; $-C_{0-2}$- alkyl-$C(=O)-N(R^{2e}, R^{3e})$; $-C_{0-2}$-alkyl-NO_2; $-C_{0-2}$-alkyl-$N(R^{2e}, R^{3e})$; $-C_{0-2}$-alkyl-$SO_2-N(R^{2e}, R^{3e})$; $-C_{0-2}$-alkyl-SO_2-R^{2e}; trihaloalkyl; $-O-C_{0-2}$-alkyl-$O-R^{2e}$; $-C_{0-2}$-alkyl-$O-R^{2e}$; $-O-C_{1-4}$-alkyl-$C(=O)-N(R^{2e}, R^{3e})$; $-O-C_{1-4}$-alkyl-$C(=O)-O-R^{2e}$; $-C_{0-2}$-alkyl-$N(R^{2e})-C(=O)-R^{3e}$; $-C_{0-2}$-alkyl-$N(-R^{2e})-SO_2-R^{3e}$; $-CH_2-N(R^{2e})-C(=O)-R^{3e}$;$-CH_2-N(R^{2e})-SO_2-R^{3e}$; $-(CH_2)_{0-6}-NR^{2e}R^{3e}$; $-C(=O)-N(R^{2e},R^{3e})$; $-N(-(CH_2)_{1-6}-OR^{2e})_2$; $-N(R^{10})-(CH_2)_{1-6}-OR^{2e}$; $-N(R^{10})-C(=O)-R^{2e}$; $-N(R^{10})-SO_2-R^{2e}$; $-C(=N(R^{10}))-N(R^{2e},R^{3e})$; and a $-(CH_2)_{0-6}$-5-6 membered saturated, partially unsaturated or aromatic heterocyclic ring containing 1-4 heteroatoms selected from N, O and S;

R^{10}, R^{2e} and R^{3e} are each independently a member selected from the group consisting of:

H; -C_{1-4}-alkyl; -C_{0-2}-alkyl-O-R^{1g}; -C_{0-2}-alkyl-N(-R^{1g}, -R^{2g});-C_{1-4}-alkyl-carbocyclic aryl; -C_{1-4}-alkyl-heterocyclic; and R^{10} and R^{2e}, or R^{2e} and R^{3e} together with the N atom to which they are attached can form 5-8 membered heterocyclic ring containing 1-4 heteroatoms selected from N, O and S which can be substituted with 0-2 R^{1g} groups;

R^{1g} and R^{2g} are indepedently a member selected from the group of:

H; halo; -C_{1-4}-alkyl, a carbocyclic aryl group; a saturated, partially unsaturated or aromatic heterocyclic group; -CN; -C(=O)-N(R^{3g},R^{4g}); -C(=O)-OR^{3g}; -NO_2; -$(CH_2)_p$-N$R^{3g}R^{4g}$; -$SO_2NR^{3g}R^{4g}$; -SO_2R^{3g}; -CF_3; and -$(CH_2)_p$OR^{3g};

p is an integer of 0-2;

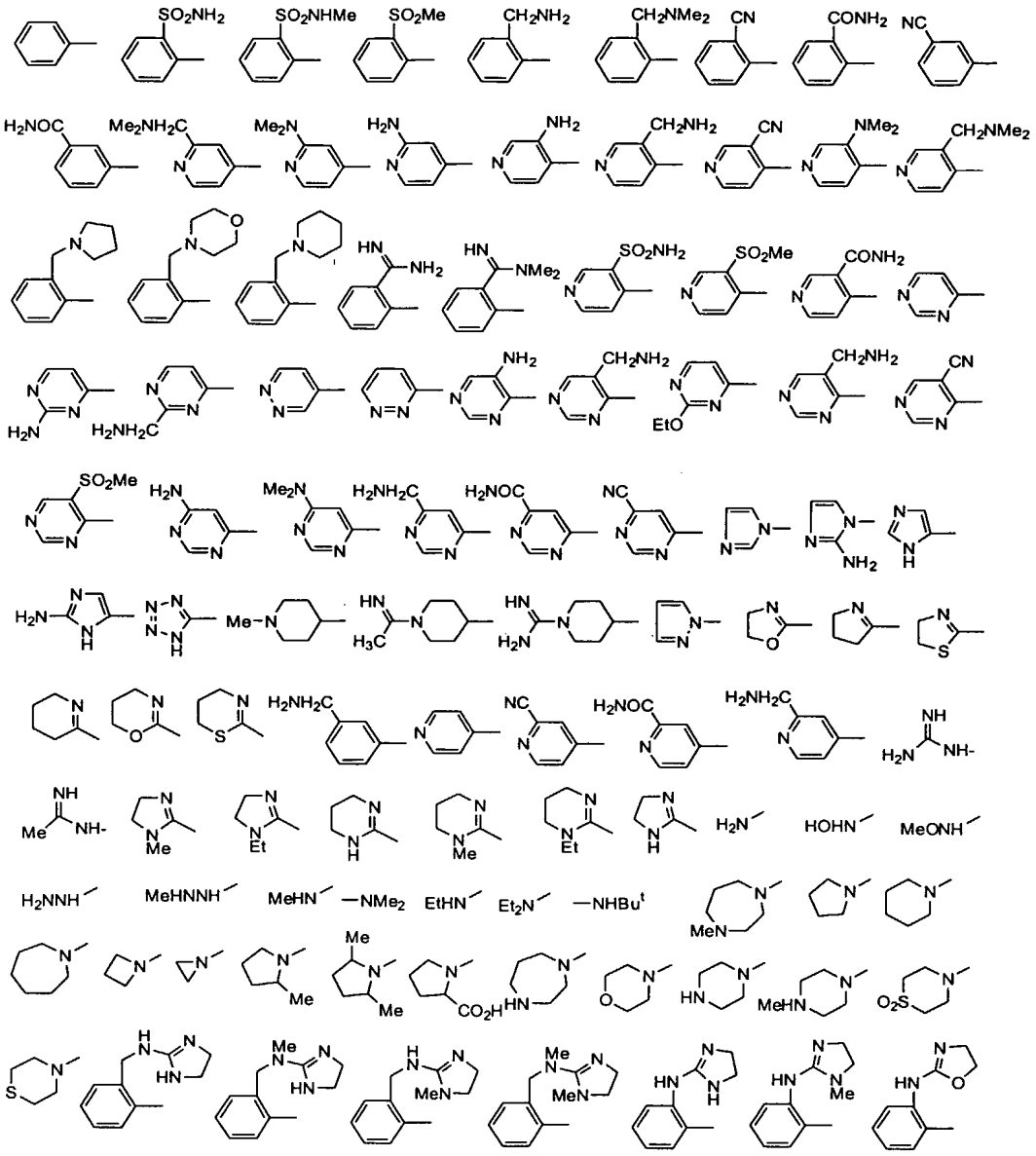
R^{3g} and R^{4g} are each independently selected from the group consisting of:

H; C_{1-4}-alkyl and -C_{0-4}-alkyl-carbocyclic aryl;

and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.

3. A compound of claim 1, wherein:

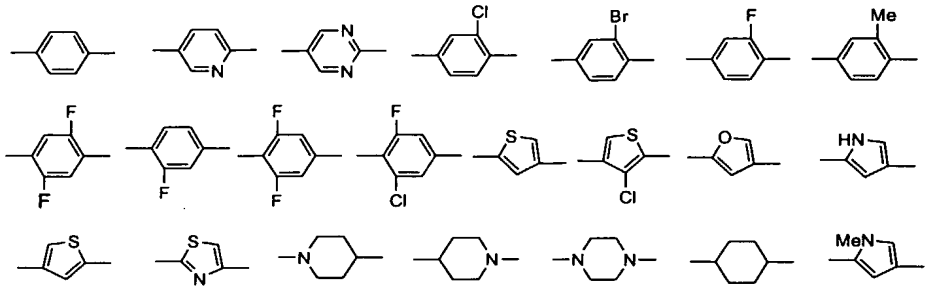
A is a member selected from the group consisting of:



Q is a member selected from the group consisting of:

a direct link, -C(=O)-, -NH-, -NMe-, -$NHCH_2$-, -$NMeCH_2$-, -C(=NH)-, -C(=NMe)-;

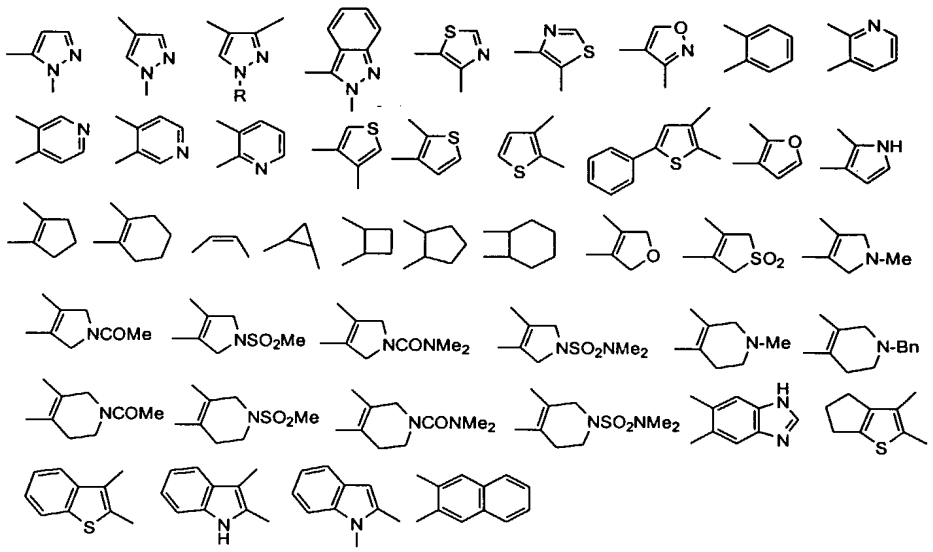
D is a direct link or is a member selected from the group consisting of:



E is a member selected from the group consisting of:

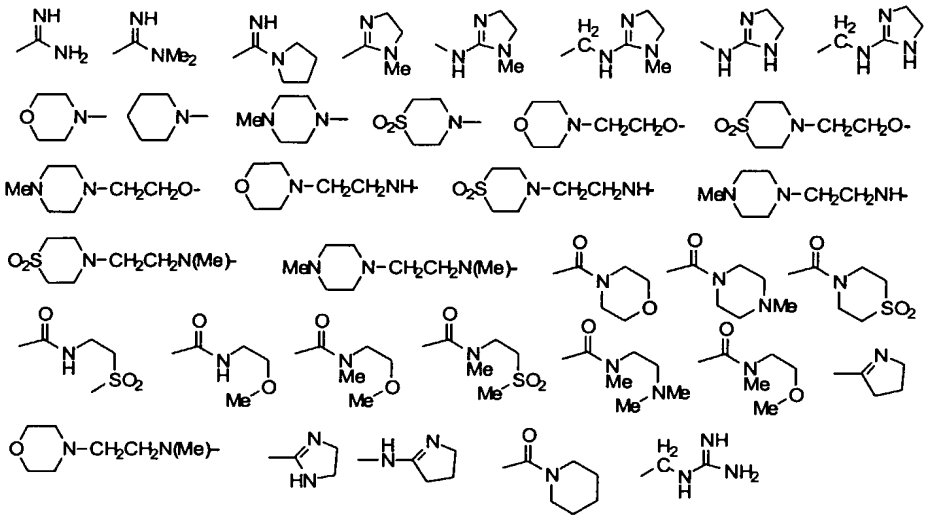
a direct link, $-CH_2NH-$, $-C(=O)-NH-$, $-NH-C(=O)-$;

G is a member selected from the group consisting of:



G is substituted by 0-4 R^{1d} groups and each R^{1d} group is independently selected from the group consisting of:

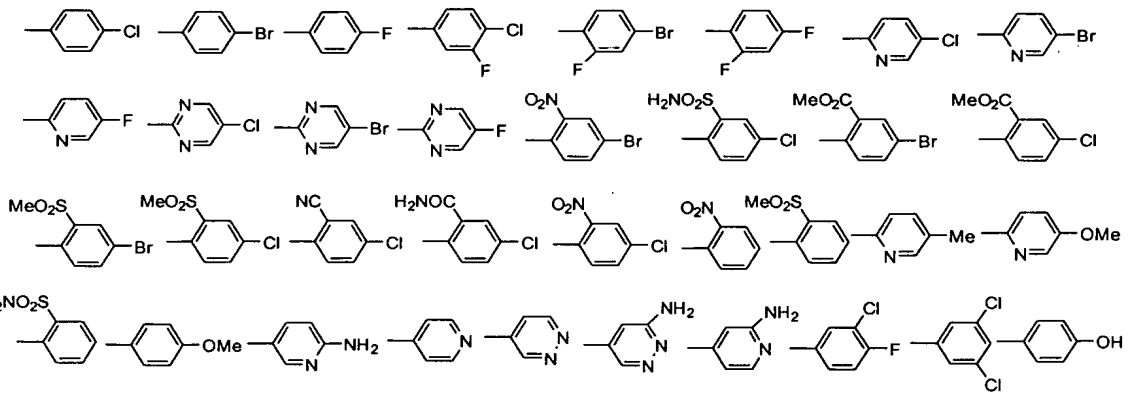
H, $-CH_3$, $-CF_3$, -Cl, -F, -Br, $-NH_2$, $-NMe_2$, -OH, -OMe, $-NHSO_2Me$, $-NO_2$, -CN, $-C(=O)-OMe$, $-CO_2H$, $-CONH_2$, $-SO_2NH_2$, $-SO_2CH_3$, $-NHC(=O)Me$, $-C(=O)N(-Me)_2$, $-CH_2NH_2$, $-CH_2N(-Me)_2$, $-CH_2OH$, $-OCH_2CO_2H$, $-OCH_2C(=O)-OMe$, $-OCH_2C(=O)-NH_2$ and $-OCH_2C(=O)N(-Me)_2$.

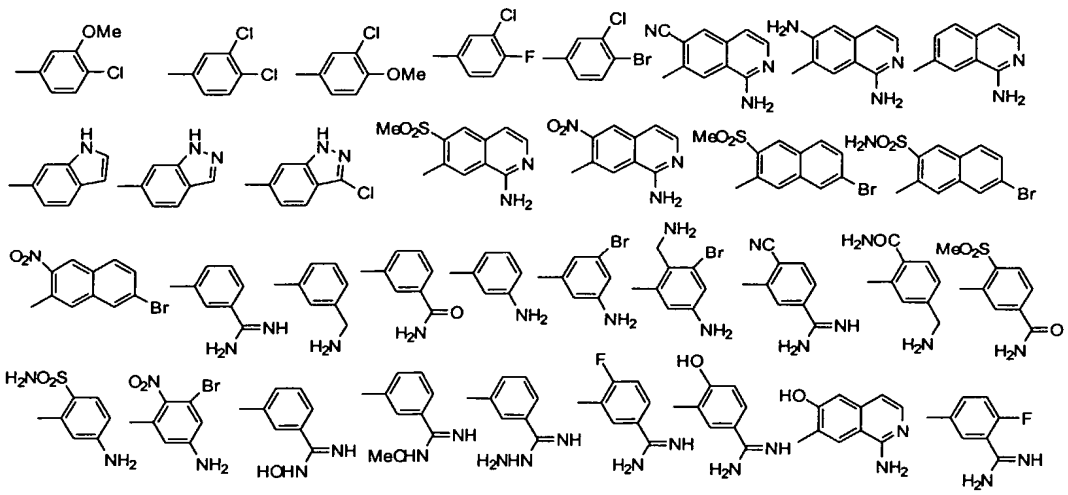


J is a member selected from the group consisting of:

a direct link, -O-, -NH-, -C(=O)-NH- and -NH-C(=O)-;

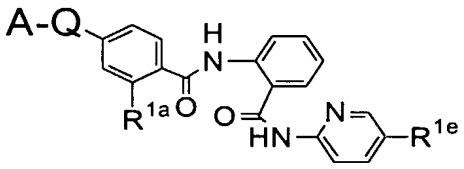
X is a member selected from the group consisting of:





and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.

4. A compound of claim 1, having the following structure:



wherein:

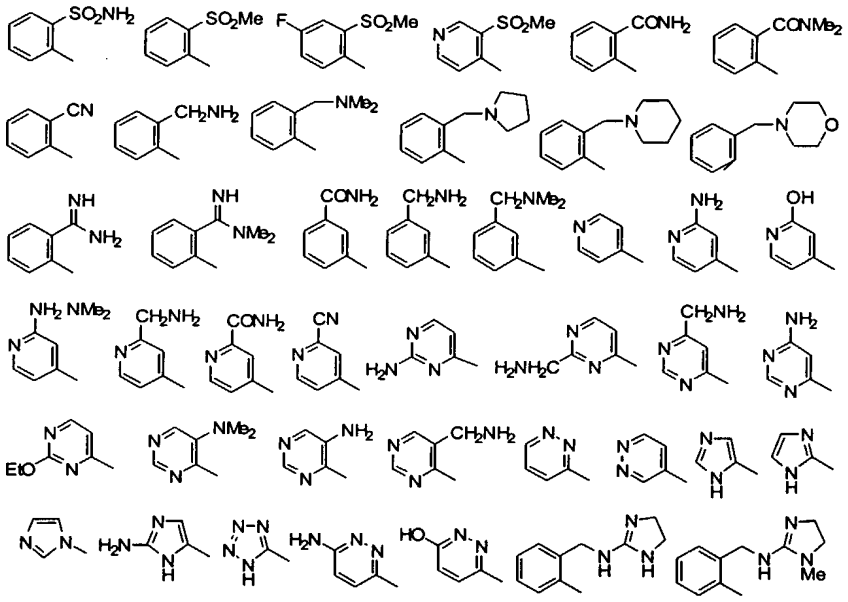
R^{1a} is a member selected from the group consisting of:

H, -F, -Cl and –Br;

R^{1e} is a member selected from the group consisting of:

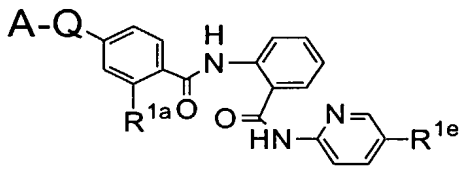
H, -F, -Cl, -Br, -OMe, -OH, -Me, $-CF_3$ and $-CH_2NH_2$; and

A-Q is a member selected from the group consisting of:



and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.

5. A compound of claim 1 having the following structure:



wherein:

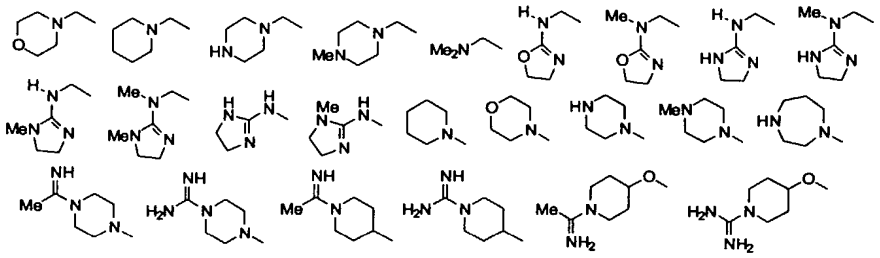
R^{1a} is a member selected from the group consisting of:

H, -F, -Cl and –Br;

R^{1e} is a member selected from the group consisting of:

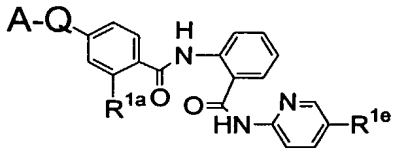
H, -F, -Cl, -Br, -OMe, -OH, -Me, $-CF_3$ and $-CH_2NH_2$; and

A-Q is a member selected from the group consisting of:



and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.

6. A compound of claim 1 having the following structure:



wherein:

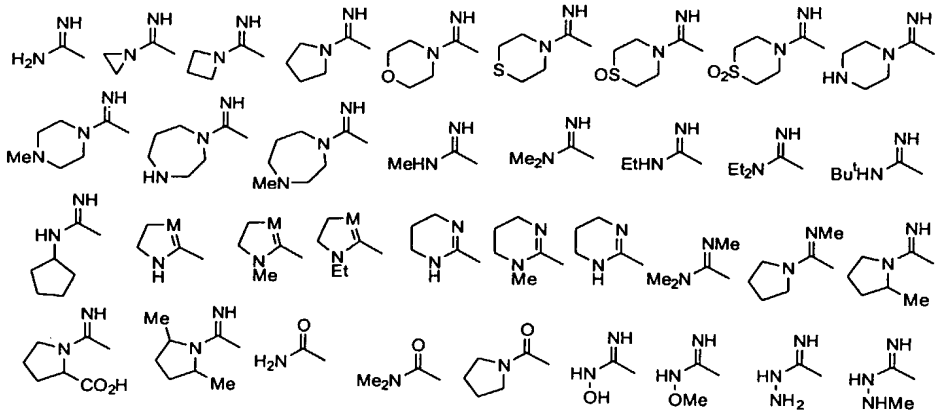
R^{1a} is a member selected from the group consisting of:

H, -F, -Cl and –Br;

R^{1e} is a member selected from the group consisting of:

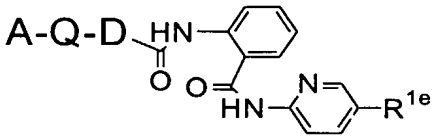
H, -F, -Cl, -Br, -OMe, -OH, -Me, $-CF_3$ and $-CH_2NH_2$;

A-Q is a member selected from the group consisting of:



and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.

7. A compound of claim 1 having the following structure:

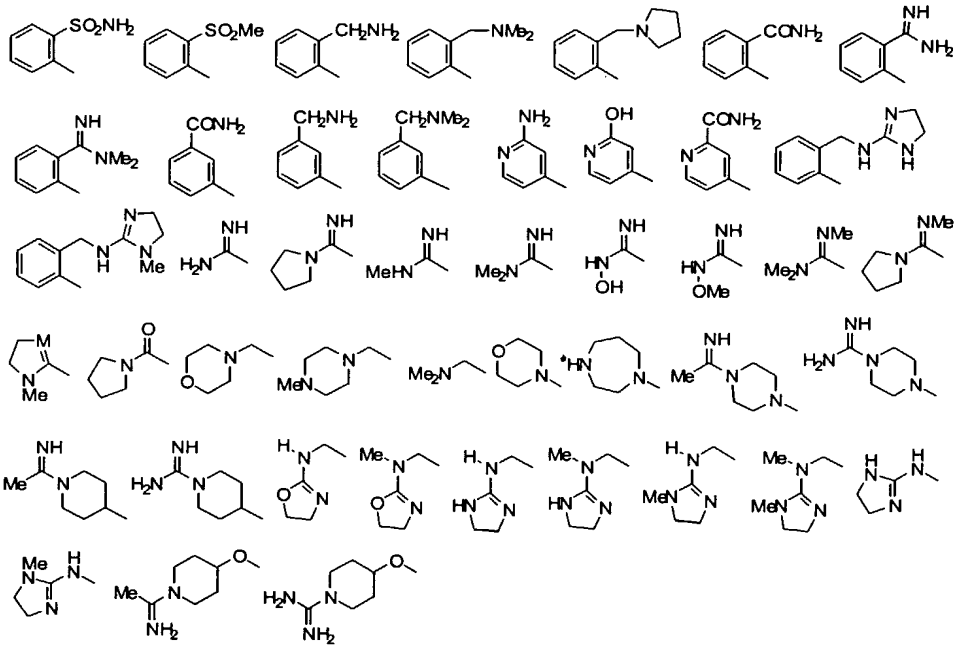


wherein:

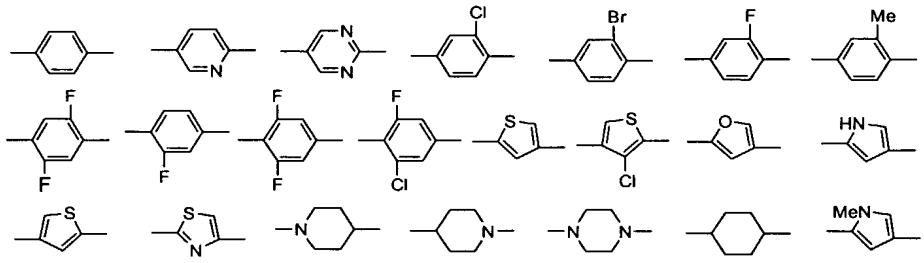
R^{1e} is a member selected from the group consisting of:

H, -F, -Cl, -Br, -OMe, -OH, -Me, $-CF_3$ and $-CH_2NH_2$;

A-Q is a member selected from the group consisting of:

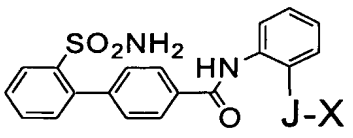


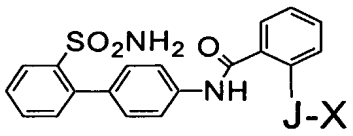
D is a member selected from the group consisting of:



and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.

8. A compound of claim 1 having the following structure:



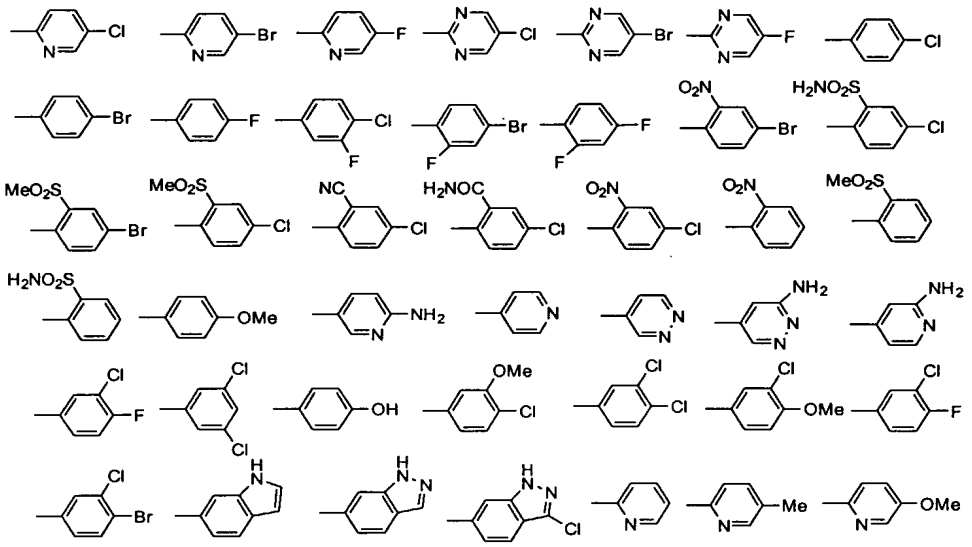


wherein:

J is a member selected from the group consisting of:

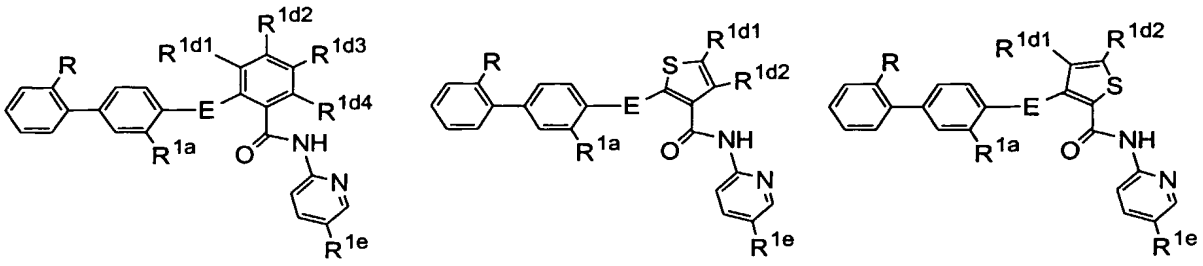
-NHC(=O)-, -C(=O)NH-;

X is a member selected from the group consisting of:



and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.

9. A compound of claim 1 having the following structure:



wherein:

R is a member selected from the group of :

$-SO_2-NH_2$ and $-SO_2Me$;

R^{1a} is a member selected from the group of:

H, -F, -Cl and Br;

E is a member selected from the group consisting of:

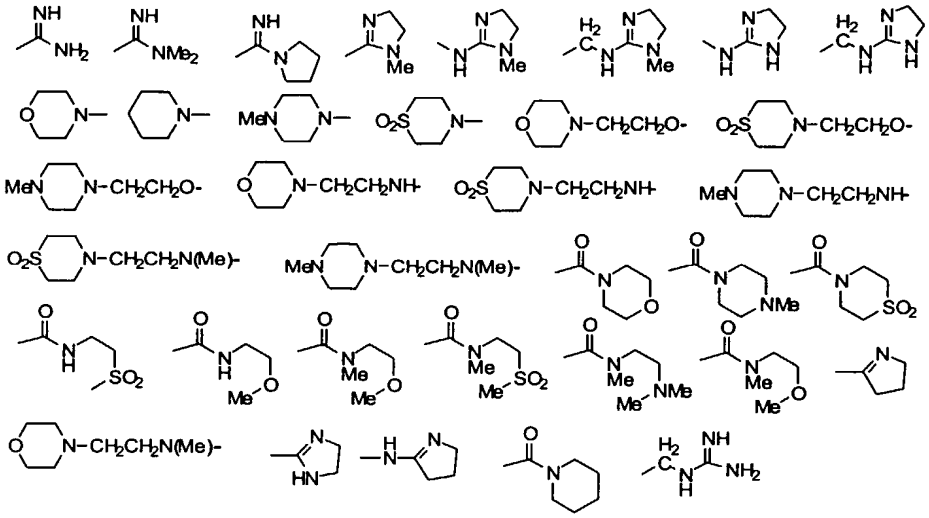
-NHC(=O)- and -C(=O)NH-;

R^{1d1}, R^{1d2}, and R^{1d4} are independently a member selected from the group of:

H, -F, -Cl, -Br, -Me, $-NO_2$, -OH, -OMe, $-NH_2$, -NHAc, $-NHSO_2Me$, $-CH_2OH$ and $-CH_2NH_2$;

R^{1d3} is a member selected from the group of:

H, $-CH_3$, $-CF_3$, -Cl, -F, -Br, $-NH_2$, $-N(-Me)_2$, -OH, -OMe, $-NHSO_2Me$, $-NO_2$, -CN, $-C(=O)-OMe$, $-CO_2H$, $-C(=O)-NH_2$, $-SO_2NH_2$, $-SO_2CH_3$, $-NHC(=O)-Me$, $-C(=O)-N(-Me)_2$, $-CH_2NH_2$, $-CH_2-N(-Me)_2$, $-CH_2OH$, $-OCH_2CO_2H$, $-OCH_2C(=O)-OMe$, $-OCH_2C(=O)-NH_2$, and $-OCH_2C(=O)-N(-Me)_2$,

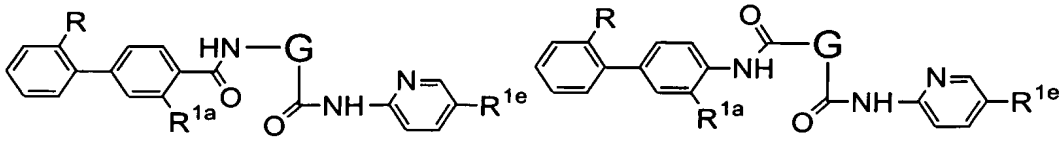


R^{1e} is a member selected from the group of :

F, -Cl, -Br, -OH, -Me and –Ome,

and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.

10. A compound of claim 1 having the following structure:



wherein:

R is a member selected from the group consisting of:

$-SO_2NH_2$, $-SO_2Me$;

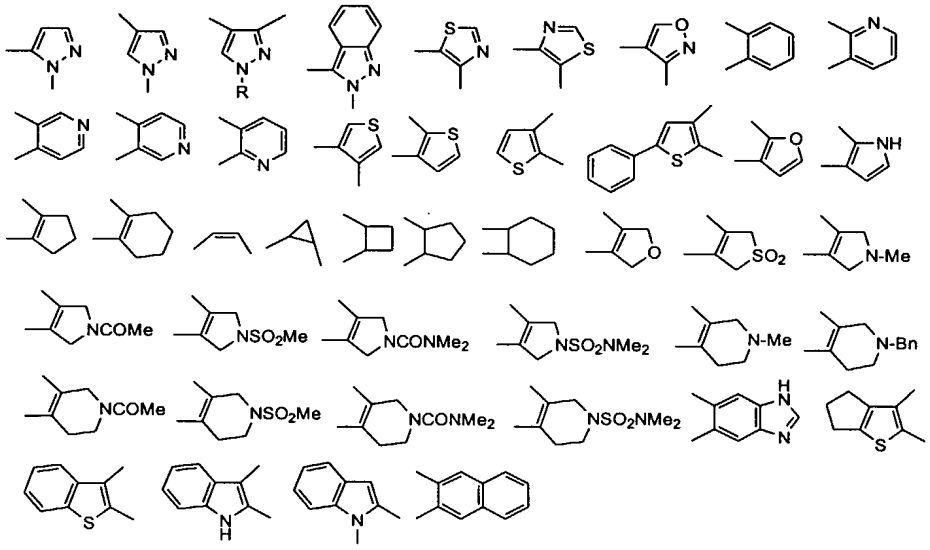
R^{1a} is a member selected from the group consisting of:

H, -F, -Cl and Br;

R^{1e} is a member selected from the group consisting of:

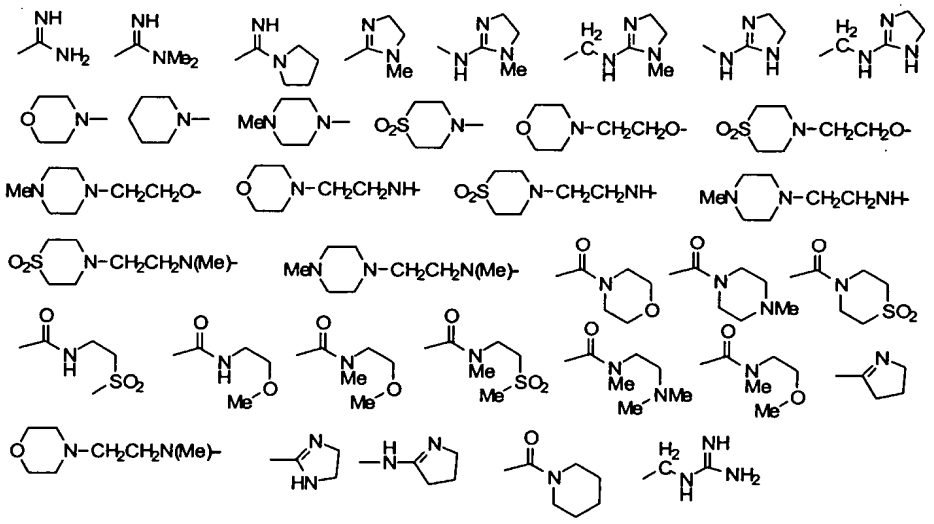
H, -F, -Cl, -Br, -OMe, -OH, -Me, $-CF_3$ and $-CH_2NH_2$; and

G is a member selected from the group consisting of:



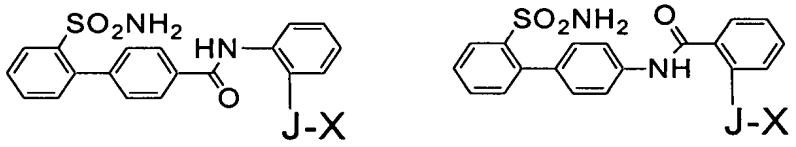
wherein each G group may be substituted by 0-4 R^{1d} groups and each such R^{1d} group is independently selected from the group consisting of:

H, $-CH_3$, $-CF_3$, -Cl, -F, -Br, $-NH_2$, $-N(-Me)_2$, -OH, -OMe, $-NHSO_2Me$, $-NO_2$, -CN, -C(=O)-OMe, $-CO_2H$, $-C(=O)-NH_2$, $-SO_2NH_2$, $-SO_2CH_3$, -NH-C(=O)-Me, $-C(=O)-N(-Me)_2$, $-CH_2NH_2$, $-CH_2-N(-Me)_2$, $-CH_2OH$, $-OCH_2CO_2H$, $-OCH_2CO_2Me$, $-OCH_2C(=O)-NH_2$, $-OCH_2C(=O)-N(-Me)_2$.



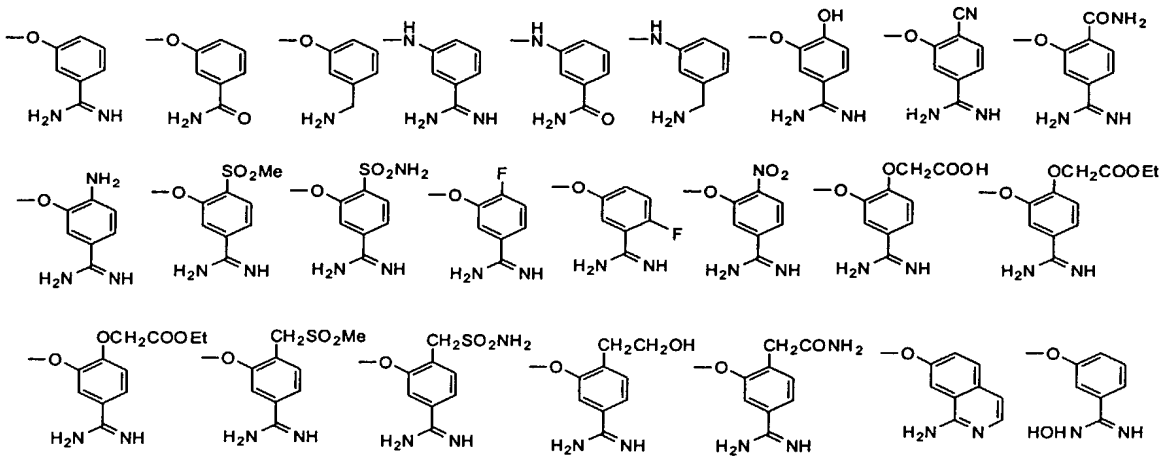
and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.

11. A compound of claim 1 having the following structure:



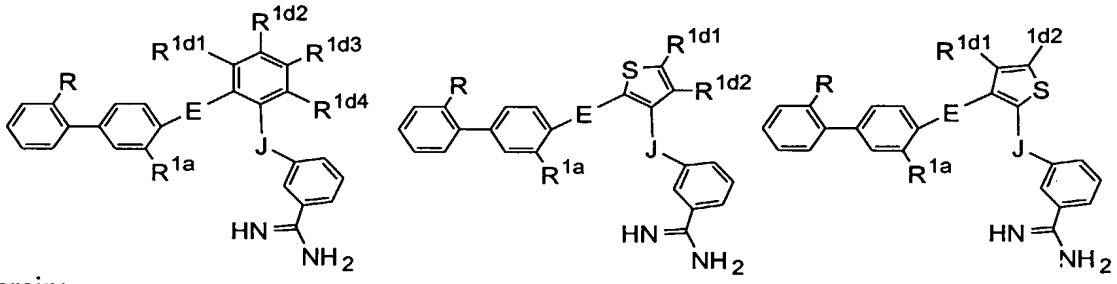
wherein:

J-X are collectively a member selected from the group consisting of:



and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.

12. A compound of claim 1 having the following structure:



wherein:

R is a member selected from the group of :

$-SO_2NH_2$, and $-SO_2Me$;

R^{1a} is a member selected from the group of:

H, -F, -Cl and Br;

E is a member selected from the group consisting of:

-NHC(=O)- and -C(=O)NH-;

J is a member selected from the group consisting of:

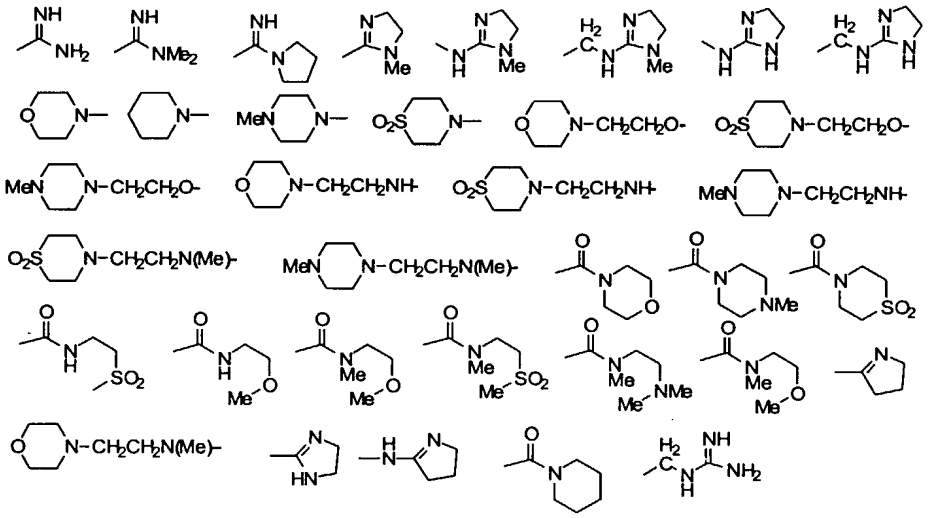
-NHC(=O)- and -C(=O)NH-, O;

R^{1d1}, R^{1d2}, and R^{1d4} are independently a member selected from the group of:

H, -F, -Cl, -Br, -Me, $-NO_2$, -OH, -OMe, $-NH_2$, -NHAc, $-NHSO_2Me$, $-CH_2OH$, $-CH_2NH_2$;

R^{1d3} is a member selected from the group of:

H, $-CH_3$, $-CF_3$, -Cl, -F, -Br, $-NH_2$, $-N(-Me)_2$, -OH, -OMe, $-NHSO_2Me$, $-NO_2$, -CN, $-CO_2Me$, $-CO_2H$, $-C(=O)-NH_2$, $-SO_2NH_2$, $-SO_2CH_3$, -NHC(=O)-Me, $-C(=O)-N(-Me)_2$, $-CH_2NH_2$, $-CH_2-N(-Me)_2$, $-CH_2OH$, $-OCH_2CO_2H$, $-OCH_2C(=O)-OMe$, $-OCH_2C(=O)-NH_2$, $-OCH_2C(=O)-N(-Me)_2$,

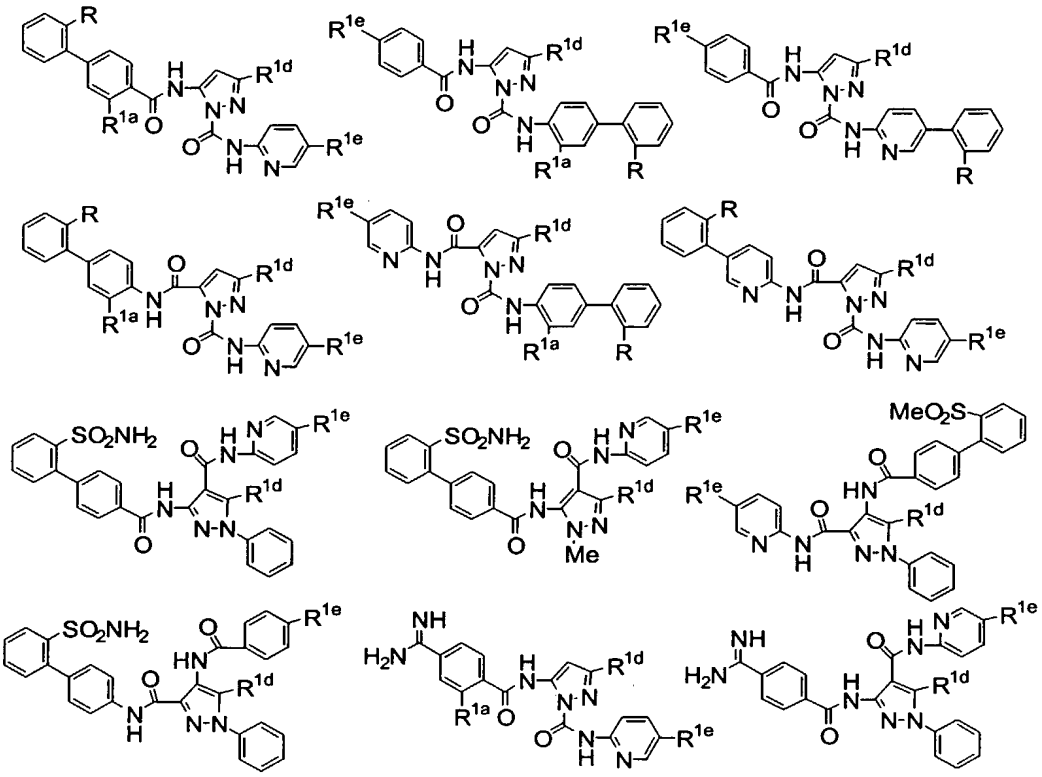


R^{1e} is a member selected from the group of :

F, -Cl, -Br, -OH, -Me and -OMe;

and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.

13. A compound of claim 1 selected from the group consisting of:



wherein:

R is a member selected from the group of :

$-SO_2-NH_2$, and $-SO_2Me$;

R^{1a} is a member selected from the group of:

H, -F, -Cl and Br;

R^{1d} is a member selected from the group consisting of:

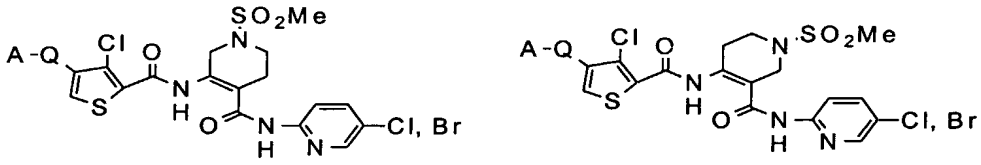
$-H$, $-CH_3$, $-CF_3$, $-CN$, $-SO_2NH_2$ and $-SO_2CH_3$; and

R^{1e} is a member selected from the group of:

-Cl and -Br;

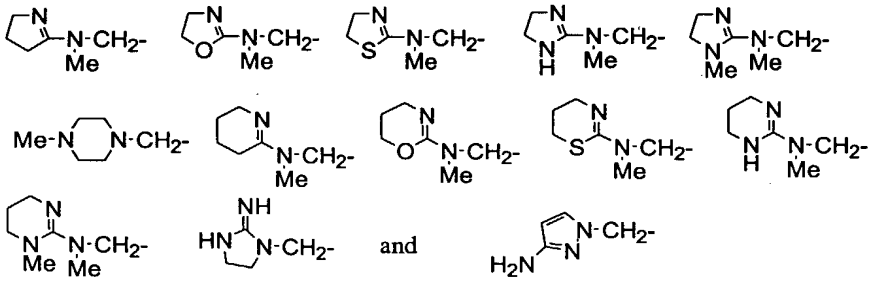
and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.

14. A compound of claim 1 having the following structure:



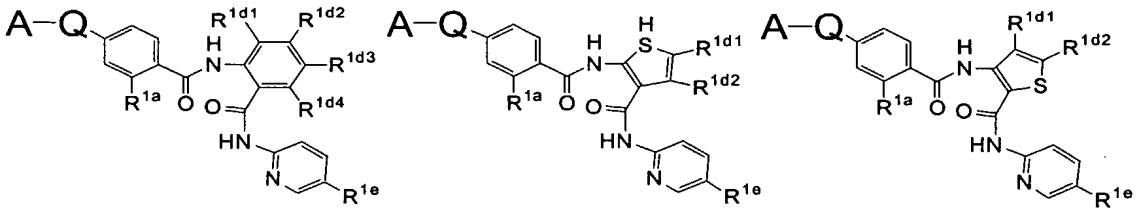
wherein:

A-Q taken together are a member selected from the group consisting of:



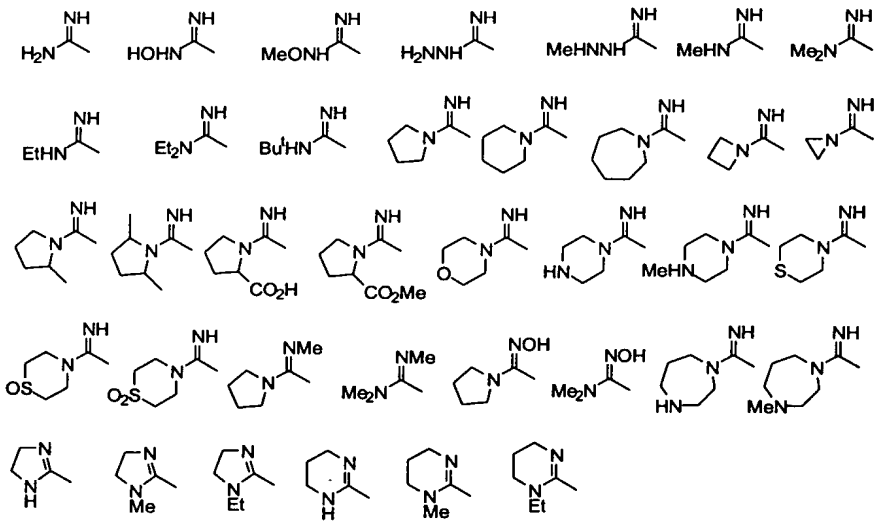
and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.

15. A compound of claim 1 selected from the group consisting of:



wherein:

A-Q is a member selected from the group of :



R^{1a} is a member selected from the group of:

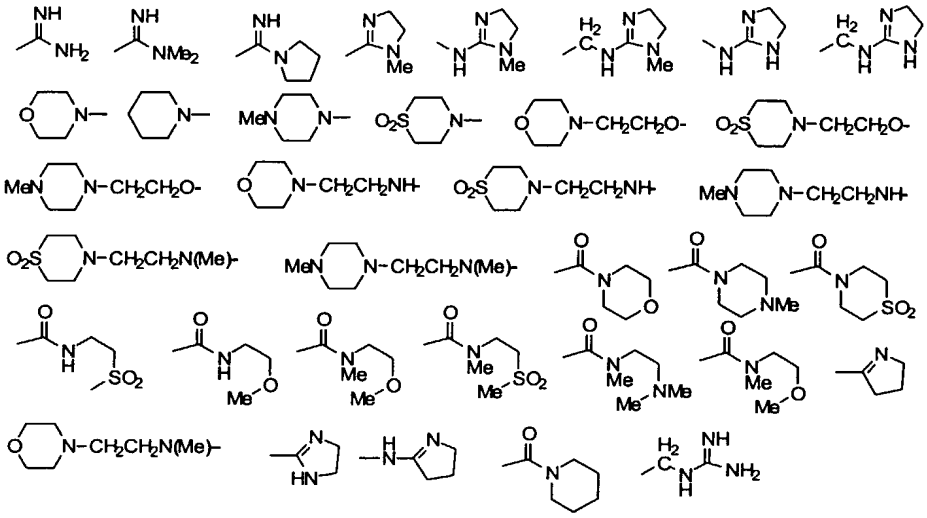
H, -F, -Cl and Br;

R^{1d1}, R^{1d2}, and R^{1d4} are independently a member selected from the group of:

H, -F, -Cl, -Br, -Me, $-NO_2$, -OH, -OMe, $-NH_2$, -NHAc, $-NHSO_2Me$, $-CH_2OH$, $-CH_2NH_2$

R^{1d3} is a member selected from the group of:

H, $-CH_3$, $-CF_3$, -Cl, -F, -Br, $-NH_2$, $-N(-Me)_2$, -OH, -OMe, $-NHSO_2Me$, $-NO_2$, -CN, -C(=O)-OMe, $-CO_2H$, -C(=O)-NH_2, $-SO_2NH_2$, $-SO_2CH_3$, -NHC(=O)-Me, -C(=O)-$N(Me)_2$, $-CH_2NH_2$, $-CH_2-N(-Me)_2$, $-CH_2OH$, $-OCH_2CO_2H$, $-OCH_2C(=O)$-OMe, $-OCH_2C(=O)-NH_2$, $-OCH_2C(=O)-N(-Me)_2$,

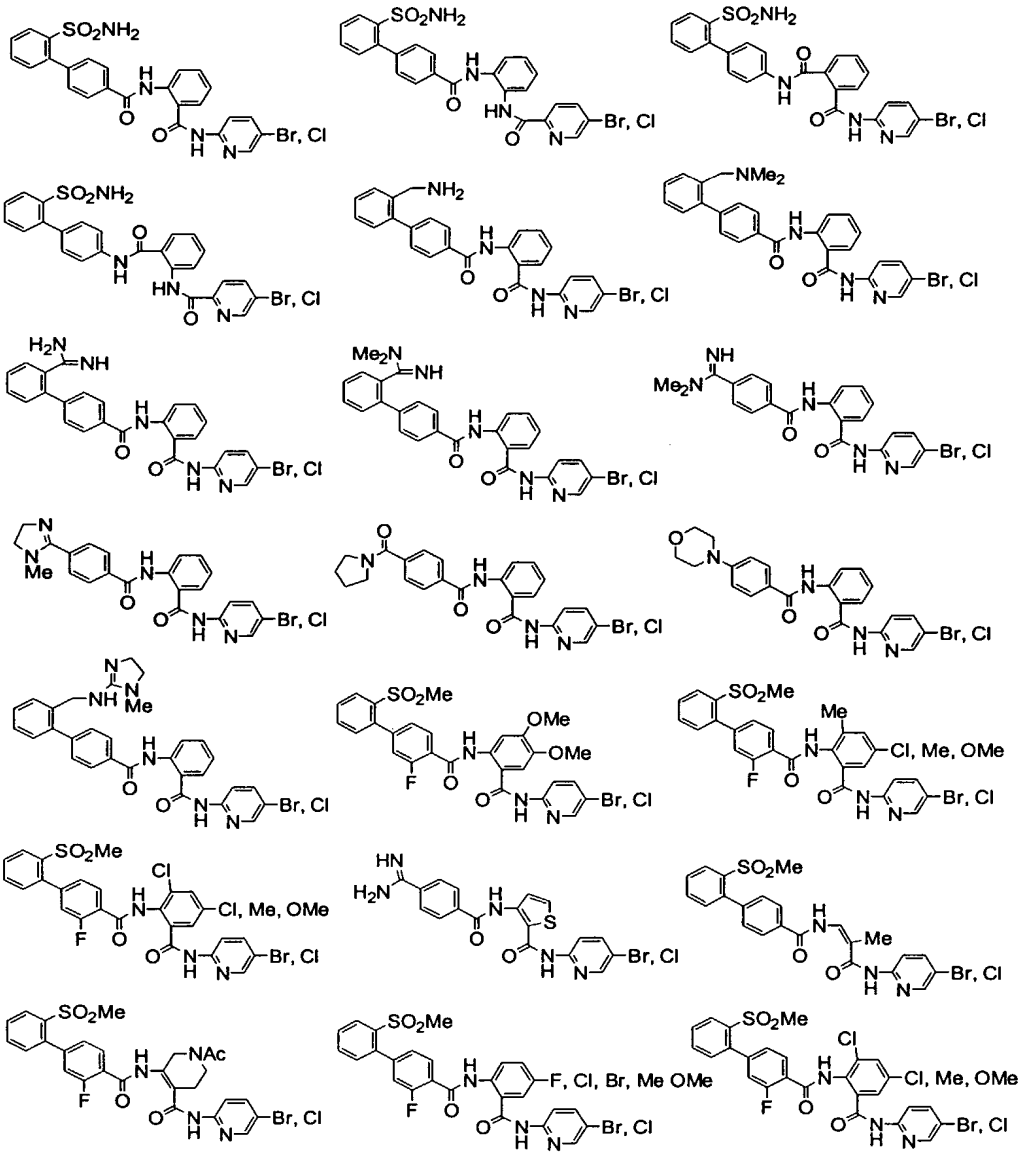


R^{1e} is a member selected from the group of:

F, -Cl, -Br, -OH, -Me and -OMe;

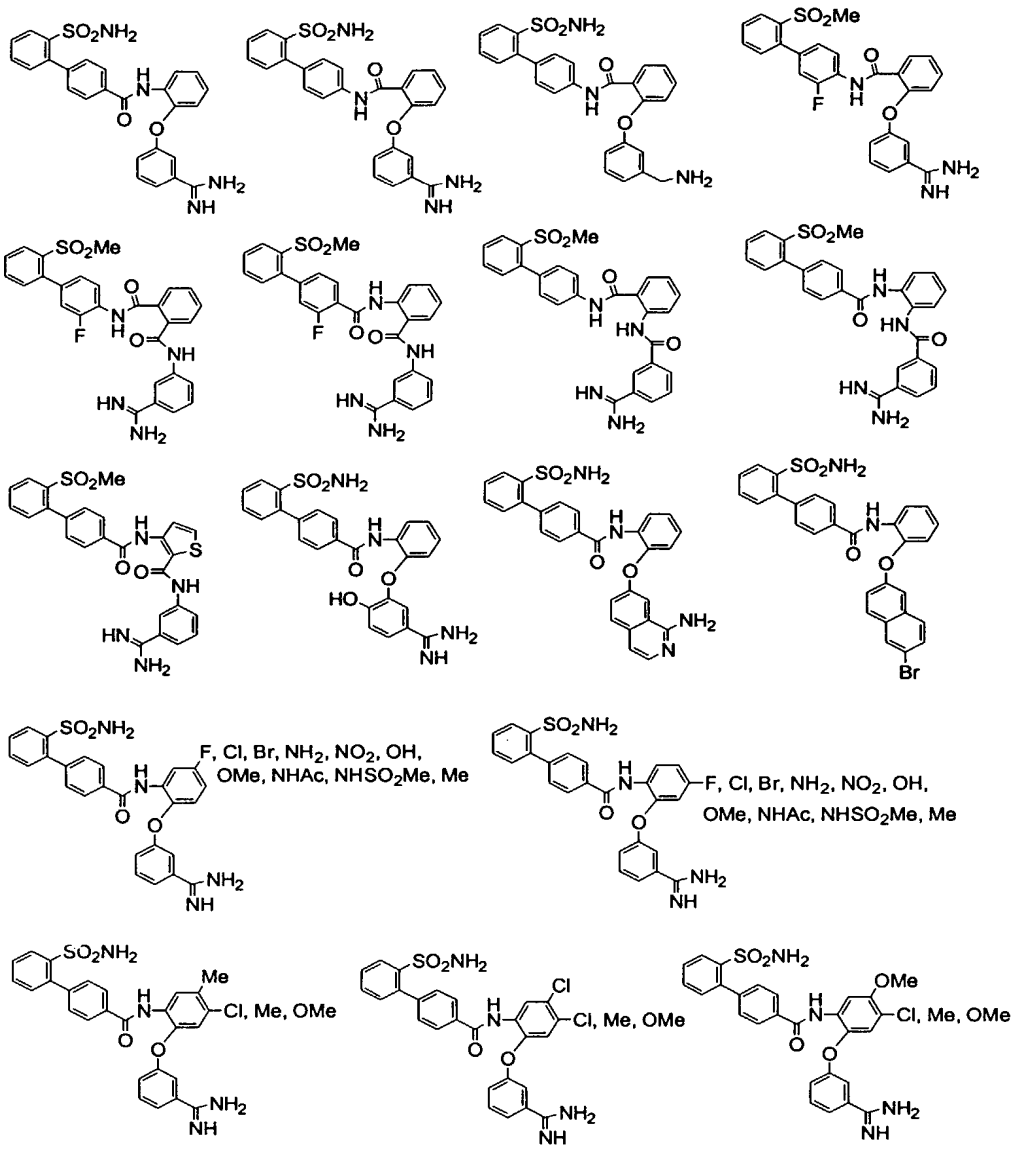
and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.

16. A compound of claim 1 selected from the group of consisting of:



and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.

17. A compound of claim 1 selected from the group consisting of:



and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.

18. A compound of claim 1 selected from the group consisting of:

3-(2-(4-[(2-aminosulfonyl)phenyl]benzoylamino) phenoxy)benzamidine, 3-(4-fluoro-2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonylamino)phenoxy) benzamidine, 3-(4-trifluoromethyl-2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonylamino)phenoxy) benzamidine, 3-(4-methylsulfonyl-2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonylamino)phenoxy) benzamidine, 3-(5-hydroxy-2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonylamino)phenoxy) benzamidine, 3-(4-methoxycarbonyl-2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonylamino)phenoxy) benzamidine, 3-(4-hydroxycarbonyl-2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonylamino)phenoxy) benzamidine, 3-(2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonylamino)pheylamino) benzamidine, 7-(2-(4-[(2-aminosulfonyl)phenyl]benzoylamino)phenoxy)-1-aminoisoquinoline, 7-(2-(4-[(2-aminosulfonyl)phenyl]benzoylamino)-4-fluorophenoxy)1-aminoisoquinoline, 7-(2-(4-[(2-aminosulfonyl)phenyl]benzoylamino)-4-trifluoromethylphenoxy)1-aminoisoquinoline, 7-(2-(4-[(2-aminosulfonyl)phenyl]benzoylamino)-4-methylsulfonylphenoxy)1-aminoisoquinoline, 3-(2-(4-[(2-aminosulfonyl)phenyl]phenylaminocarbonyl-4-nitrophenoxy) benzamidine, 3-(2-(4-[(2-aminosulfonyl)phenyl]phenylaminocarbonyl-4-aminophenoxy) benzamidine, 3-(2-(4-[(2-aminosulfonyl)phenyl]phenylaminocarbonyl-4-chlorophenoxy) benzamidine, 3-(2-(4-[(2-aminosulfonyl)phenyl]phenylaminocarbonyl-4-bromophenoxy) benzamidine, 2-bromo-6-(2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonylamino)phenoxy naphthalene, 3-methoxycarbonyl-2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonylamino)phenoxy naphthalene, 3-hydroxycarbonyl-2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonylamino)phenoxy naphthalene, 3-aminocarbonyl-2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonylamino)phenoxy naphthalene, 3-methoxycarbonyl-2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonylamino)phenoxy-6-bromo naphthalene, 3-hydroxycarbonyl-2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonylamino)phenoxy-6-bromo naphthalene, N-(5-bromo-2-pyridinyl)-(2-4-[(2-aminosulfonyl)phenyl]phenylcarbonylamino)phenylcarboxamide, N-(5-chloro-2-pyridinyl)-(2-4-[(2-aminosulfonyl)phenyl]phenylcarbonylamino)phenylcarboxamide, N-(5-bromo-2-pyridinyl)-(2-(4-[(2-methylsulfonyl)phenyl]phenylcarbonyl)amino)phenylcarboxamide,

N-(5-chloro-2-pyridinyl)-(2-(4-[(2-methylsulfonyl)phenyl]phenylcarbonyl)amino)phenylcarboxamide, N-(4-bromo-2-methoxycarbonyphenyl)-(2-(4-[(2-methylsulfonyl)phenyl]phenylcarbonyl)amino)phenylcarboxamide, N-(4-chloro-2-methoxycarbonyphenyl)-(2-(4-[(2-methylsulfonyl)phenyl]phenylcarbonyl)amino)phenylcarboxamide, N-(5-bromo-2-pyridinyl)-(2-4-[(2-aminosulfonyl)phenyl]phenylcarbonylamino)pyridinyl-3-carboxamide,
N-(5-chloro-2-pyridinyl)-(2-4-[(2-aminosulfonyl)phenyl]phenylcarbonylamino)pyridinyl-3-carboxamide, N-(5-bromo-2-pyridinyl)-(3-4-[(2-aminosulfonyl)phenyl]phenylcarbonylamino)pyridinyl-2-carboxamide, N-(5-chloro-2-pyridinyl)-(2-4-[(2-aminosulfonyl)phenyl]phenylcarbonylamino)pyridinyl-3-carboxamide, N-(4-bromo-2-nitrophenyl)-(2-(4-[(2-methylsulfonyl)phenyl]phenylcarbonyl)amino)phenylcarboxamide, N-(4-bromophenyl)-N'-(4-[(2-aminosulfonyl)phenyl]phenyl)-maleamic amide, N^1-(5-bromopyridin-2-yl)-N^4-(4-[(2-aminosulfonyl)phenyl] phenyl)-2-methylmaleamic amide, N^1-(5-bromopyridin-2-yl)-N^4-(4-[(2-aminosulfonyl)phenyl]phenyl)-3-methylmaleamic amide, N-(5-bromo-2-pyridinyl)-(2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonyl)amino)-4-nitrophenylcarboxamide, N-(5-bromo-2-pyridinyl)-(2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonyl)amino)-4-aminophenylcarboxamide, N-(5-chloro-2-pyridinyl)-(2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonyl)amino)-4-aminophenylcarboxamide, N-(5-bromo-2-pyridinyl)-(2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonyl)amino)-4-methylsulfonylaminophenylcarboxamide, N-(5-chloro-2-pyridinyl)-(2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonyl)amino)-4-methylsulfonylaminophenylcarboxamide, N-(5-bromo-2-pyridinyl)-(2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonyl)amino)-5-aminophenylcarboxamide, N-(5-chloro-2-pyridinyl)-(2-(4-[(2-aminosulfonyl)phenyl]phenylcarbonyl)amino)-5-aminophenylcarboxamide, N-(5-bromo-2-pyridinyl)-(2-(4-amidinophenylcarbonyl)amino)-phenylcarboxamide, N-(5-bromo-2-pyridinyl)-(2-(4-(2-imidazolinyl)phenylcarbonyl)amino)-phenylcarboxamide, N-(5-bromo-2-pyridinyl)-(2-(4-(5-tetrazolyl)phenylcarbonyl)amino)-phenylcarboxamide, N-(5-bromo-2-pyridinyl)-(2-(4[-[1,1-doxo(1,4-thiazaperhydroin-4-yl))iminimethy]phenylcarbonyl)amino)-phenylcarboxamide, N-(5-bromo-2-

pyridinyl)-(2-(4-[1-oxo(1,4-thiazaperhydroin-4-yl))iminimethy]phenylcarbonyl)amino)-phenylcarboxamide, N-(5-bromo-2-pyridinyl)-(2-4-[(2-aminosulfonyl)phenyl]phenylcarbonylamino)-4,5-difluorophenylcarboxamide, 3-(2-(4-[(2-aminosulfonyl)phenyl]-2-fluorophenylaminocarbonyl-4-aminophenoxy) benzamidine, 3-(2-(4-[(2-aminosulfonyl)phenyl]-2-fluorophenylaminocarbonyl-4-aminophenoxy) benzamidine, 3-(2-(4-[(2-aminosulfonyl)phenyl]benzoylamino) phenoxy)benzylamine, 2-[4-(N-{2-[N-(5-chloro-2-pyridyl)carbamoyl]phenyl}carbamoyl)phenyl]-benzenecarboxamidine, (4-{2-[(dimethylamino)iminomethyl]phenyl}phenyl)-N-{2-[N-(5-chloro(2-pyridyl))carbamoyl]phenyl}carboxamide, N-{2-[N-(5-chloro(2-pyridyl))carbamoyl]phenyl} {4-[2-((hydroxyamino)iminomethyl)-phenyl]phenyl}carboxamide, 2-[4-(N-{2-[N-(5-chloro-2-pyridyl)carbamoyl]phenyl}carbamoyl)phenyl]benzamide, {4-[2-(aminomethyl)phenyl]phenyl}-N-{2-[N-(5-chloro(2-pyridyl))carbamoyl]-phenyl}carboxamide, [4-(aminomethyl)phenyl]-N-{2-[N-(5-chloro(2-pyridyl))carbamoyl]phenyl}carboxamide, N-{2-[N-(5-chloro(2-pyridyl))carbamoyl]phenyl} {4-[(2-imidazolin-2-ylamino)methyl]-phenyl}carboxamide, N-{2-[N-(5-chloro(2-pyridyl))carbamoyl]phenyl}(4-{[(1-methyl(2-imidazolin-2-yl))amino]methyl}phenyl)carboxamide, N-{2-[N-(5-chloro(2-pyridyl))carbamoyl](3-thienyl)}[4-(1-methyl(2-imidazolin-2-yl))phenyl]carboxamide, {4-[(dimethylamino)iminomethyl]phenyl}-N-{2-[N-(5-chloro(2-pyridyl))carbamoyl](3-thienyl)}carboxamide, 4-(N-{2-[N-(5-chloro-2-pyridyl)carbamoyl]-3-thienyl}carbamoyl)benzenecarboxamidine, N-{2-[N-(5-chloro(2-pyridyl))carbamoyl](3-thienyl)}[4-(iminopiperidylmethyl)-phenyl]carboxamide, N-{2-[N-(5-chloro(2-pyridyl))carbamoyl](3-thienyl)}[4-(iminopyrrolidinylmethyl)-phenyl]carboxamide, N-{2-[N-(5-chloro(2-pyridyl))carbamoyl](3-thienyl)}[4-(iminomorpholin-4-ylmethyl)phenyl]carboxamide, N-{2-[N-(5-chloro(2-pyridyl))carbamoyl](3-thienyl)}[4-(imino-1,4-thiazaperhydroin-4-ylmethyl)phenyl]carboxamide, [4-(azaperhydroepinyliminomethyl)phenyl]-N-{2-[N-(5-chloro(2-pyridyl))carbamoyl](3-thienyl)}carboxamide, N-{2-[N-(5-chloro(2-pyridyl))carbamoyl](3-thienyl)} {4-[imino(2-methylpyrrolidinyl)methyl]phenyl}carboxamide, N-{2-[N-(5-chloro(2-pyridyl))carbamoyl](3-thienyl)} {4-[imino(methylamino)methyl]-phenyl}carboxamide, N-{2-[N-(5-chloro(2-pyridyl))carbamoyl](3-thienyl)}[4-(3-methyl(3,4,5,6-tetrahydropyrimidin-2-yl))phenyl]carboxamide, N-{2-[N-(5-chloro(2-

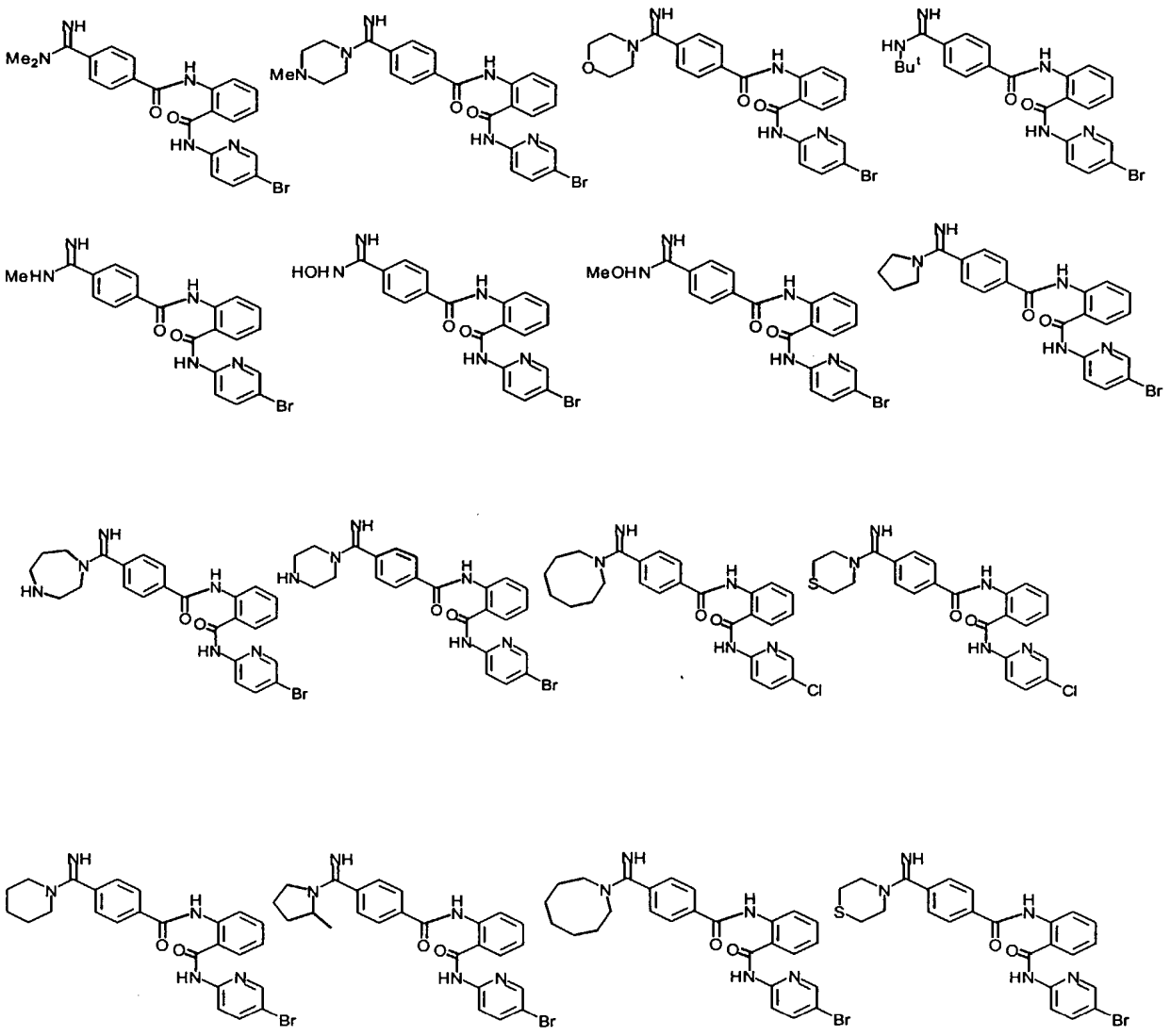
pyridyl))carbamoyl](3-thienyl)}[4-((hydroxyamino)iminomethyl)-phenyl]carboxamide, 1-{[4-(N-{2-[N-(5-chloro(2-pyridyl))carbamoyl](3-thienyl)}carbamoyl)phenyl]-iminomethyl}pyrrolidine-2-carboxylic acid, N-{2-[N-(5-bromo(2-pyridyl))carbamoyl](3-thienyl)}[4-(1-methyl(2-imidazolin-2-yl))phenyl]carboxamide, 4-(N-{2-[N-(5-bromo-2-pyridyl)carbamoyl]-3-thienyl}carbamoyl)benzenecarboxamidine, N-{2-[N-(5-bromo(2-pyridyl))carbamoyl](3-thienyl)}[4-(iminopyrrolidinylmethyl)phenyl]carboxamide, N-{2-[N-(5-bromo(2-pyridyl))carbamoyl](3-thienyl)}[4-(iminopiperidylmethyl)phenyl]carboxamide, N-{2-[N-(5-bromo(2-pyridyl))carbamoyl](3-thienyl)}[4-(iminomorpholin-4-ylmethyl)phenyl]carboxamide, N-{2-[N-(5-bromo(2-pyridyl))carbamoyl](3-thienyl)}[4-(imino-1,4-thiazaperhydroin-4-ylmethyl)phenyl]carboxamide, N-{3-[N-(5-chloro(2-pyridyl))carbamoyl](2-thienyl)}[4-(iminopyrrolidinylmethyl)phenyl]carboxamide, N-{3-[N-(5-chloro(2-pyridyl))carbamoyl](2-thienyl)}[4-(1-methyl(2-imidazolin-2-yl))phenyl]carboxamide, 3-[(3-{[4-(2-sulfamoylphenyl)phenyl]carbonylamino}-2-thienyl)carbonylamino]benzenecarboxamidine, N-{2-[N-(5-chloro(2-pyridyl))carbamoyl](3-thienyl)}[4-(2-sulfamoylphenyl)phenyl]carboxamide, N-{2-[N-(5-bromo(2-pyridyl))carbamoyl](3-thienyl)}[4-(2-sulfamoylphenyl)phenyl]carboxamide, N-(5-bromo-2-pyridinyl)-(2-4-[(2-aminosulfonyl)phenyl]phenylaminocarbonyl)5-methyl-pyrazolcarboxamide, N-(5-bromo-2-pyridinyl)-(2-4-[(2-aminosulfonyl)phenyl]phenylcarbonylamino)-5-fluorophenylcarboxamide, N-(5-bromo-2-pyridinyl)-(2-4-[(2-aminosulfonyl)phenyl]phenylaminocarbonylamino)-5-fluorophenylcarboxamide, N-(5-bromo-2-pyridinyl)-(2-(4-amidinophenylcarbonyl)amino)5-fluorophenylcarboxamide, N-(5-bromo-2-pyridinyl)-(2-(4-(1-methyl-2-imadazolin-2-yl)phenylcarbonyl)amino)5-fluorophenylcarboxamide, N-{2-[N-(5-bromo(2-pyridyl))carbamoyl]-4,5-dimethoxyphenyl}(4-cyanophenyl)carboxamide, (4,5-dimethoxy-2-{[4-(1-methyl(2-imidazolin-2-yl))phenyl]carbonylamino}phenyl)-N-(5-bromo(2-pyridyl))carboxamide, 4-(N-{2-[N-(5-bromo(2-pyridyl))carbamoyl]-4,5-dimethoxyphenyl}carbamoyl)-benzenecarboxamidine, N-(5-chloro(2-pyridyl)){2-[(4-cyanophenyl)carbonylamino]-5-methoxyphenyl}-carboxamide, N-(5-chloro(2-pyridyl))(5-methoxy-2-{[4-(1-methyl(2-imidazolin-2-yl))phenyl]-carbonylamino}phenyl)carboxamide, 4-(N-{2-[N-(5-chloro(2-pyridyl))carbamoyl]-4-methoxyphenyl}carbamoyl)benzene-carboxamidine, N-(5-chloro(2-pyridyl))[2-({4-[imino(methylamino)methyl]phenyl}carbonylamino)-5-methoxyphenyl]carboxamide,

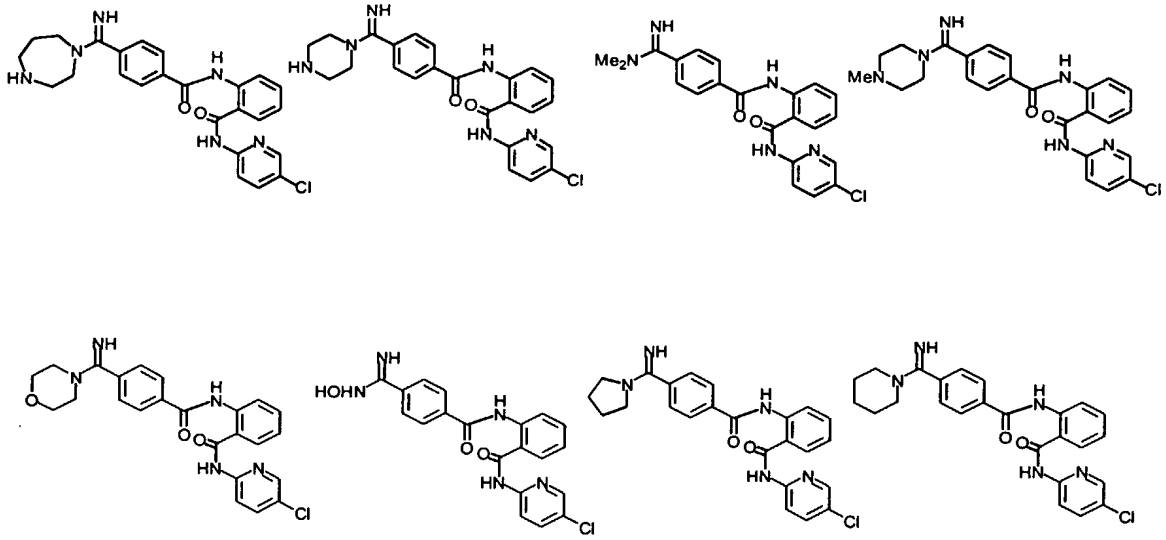
[2-({4-[(dimethylamino)iminomethyl]phenyl}carbonylamino)-5-methoxyphenyl]-N-(5-chloro(2-pyridyl))carboxamide, N-(5-chloro(2-pyridyl))(2-{[4-(iminopyrrolidinylmethyl)phenyl]carbonylamino}-5-methoxyphenyl)carboxamide, N-(5-chloro(2-pyridyl))(2-{[4-(iminopiperidylmethyl)phenyl]carbonylamino}-5-methoxyphenyl)carboxamide, N-(5-chloro(2-pyridyl))(2-{[4-(iminomorpholin-4-ylmethyl)phenyl]carbonylamin}-5-methoxyphenyl)carboxamide, N-(5-chloro(2-pyridyl))(2-{[4-(imino-1,4-thiazaperhydroin-4-ylmethyl)phenyl]carbonylamino}-5-methoxyphenyl)carboxamide, (2-{[4-(amino(hydroxyimino)methyl)phenyl]carbonylamino}-5-methoxyphenyl)-N-(5-chloro(2-pyridyl))carboxamide, N-(5-bromo(2-pyridyl)){2-[(4-cyanophenyl)carbonylamino]-5-methoxyphenyl}carboxamide, N-(5-bromo(2-pyridyl))(5-methoxy-2-{[4-(1-methyl(2-imidazolin-2-yl))phenyl]carbonylamino}phenyl)carboxamide, 4-(N-{2-[N-(5-bromo(2-pyridyl))carbamoyl]-4-methoxyphenyl}carbamoyl)benzenecarboxamidine, N-(5-bromo(2-pyridyl))[2-({4-[imino(methylamino)methyl]phenyl}carbonylamino)-5-methoxyphenyl]carboxamide, [2-({4-[(dimethylamino)iminomethyl]phenyl}carbonylamino)-5-methoxyphenyl]-N-(5-bromo(2-pyridyl))carboxamide, N-(5-chloro(2-pyridyl))(2-{[4-(iminopyrrolidinylmethyl)phenyl]carbonylamino}-5-methoxyphenyl)carboxamide, N-(N-(5-bromo(2-pyridyl))(2-{[4-(iminopiperidylmethyl)phenyl]carbonylamino}-5-methoxyphenyl)carboxamide, N-(5-bromo(2-pyridyl))(2-{[4-(iminomorpholin-4-ylmethyl)phenyl]carbonylamino}-5-methoxyphenyl)carboxamide, N-(5-bromo(2-pyridyl))(2-{[4-(imino-1,4-thiazaperhydroin-4-ylmethyl)phenyl]carbonylamino}-5-methoxyphenyl)carboxamide, (2-{[4-(amino(hydroxyimino)methyl)phenyl]carbonylamino}-5-methoxyphenyl)-N-(5-bromo(2-pyridyl))carboxamide, N-(5-chloro(2-pyridyl)){6-[(4-cyanophenyl)carbonylamino]-3-hydroxyphenyl}carboxamide, ethyl 2-{3-[N-(5-chloro(2-pyridyl))carbamoyl]-4-[(4-cyanophenyl)carbonylamino]-phenoxy}acetate, methyl 2-[4-({4-[(dimethylamino)iminomethyl]phenyl}carbonylamino)-3-[N-(5-chloro(2-pyridyl))carbamoyl]phenoxy]acetate, (6-{[4-(amino(hydroxyimino)methyl)phenyl]carbonylamino}-3-hydroxyphenyl)-N-(5-chloro(2-pyridyl))carboxamide, 4-(N-{2-[N-(5-chloro(2-pyridyl))carbamoyl]-4-hydroxyphenyl}carbamoyl)-benzenecarboxamidine, and 4-(N-{2-[N-(5-chloro(2-pyridyl))carbamoyl]-4-hydroxyphenyl}carbamoyl)-benzenecarboxamidine,

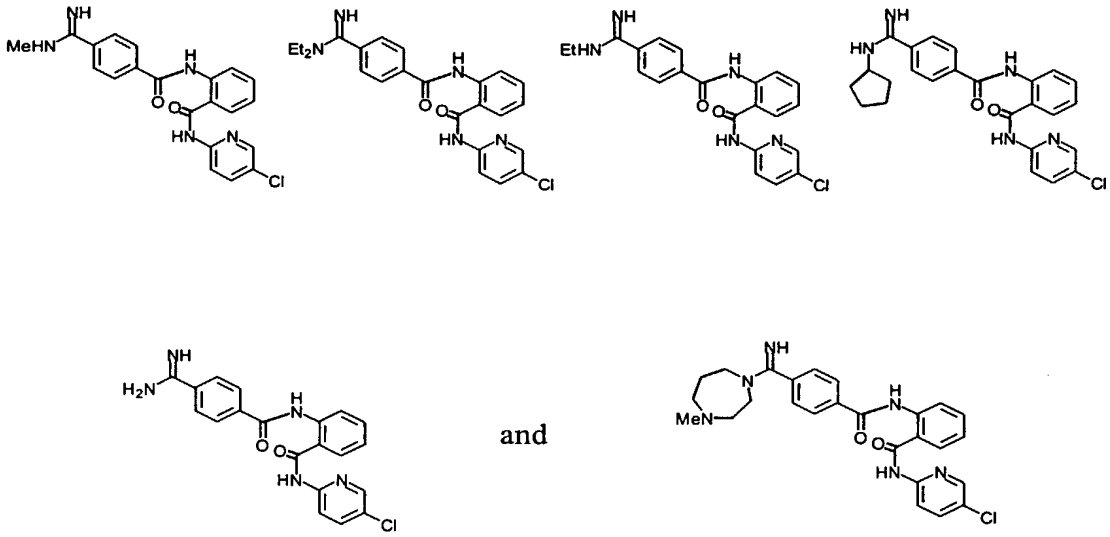
and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.

19. The compound according to claim 1 selected from the group consisting of:

5



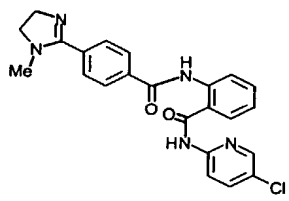
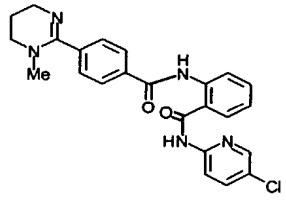
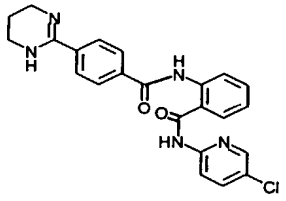
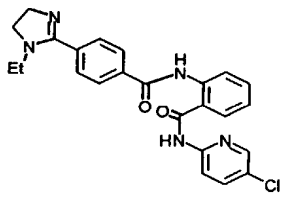


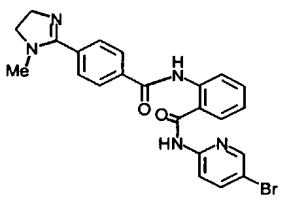
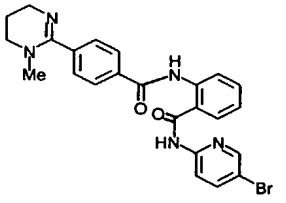
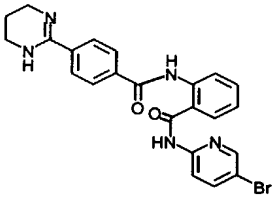
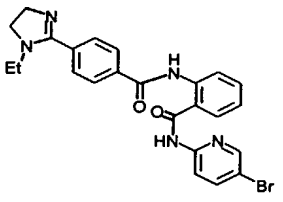


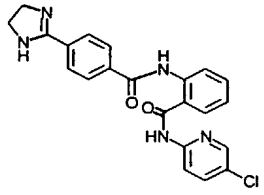
and

and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.

20. The compound according to claim 1 selected from the group consisting of:

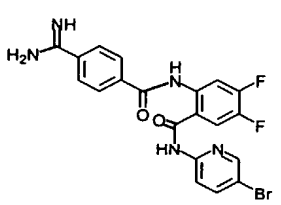
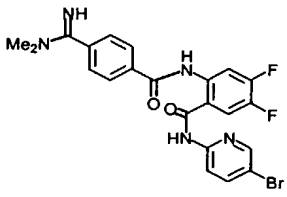
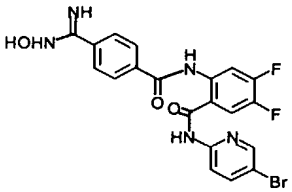
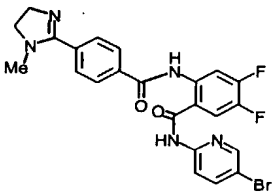





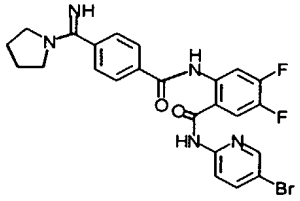





and 

and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.

21. The compound according to claim 1 selected from the group consisting of: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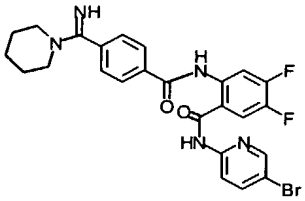
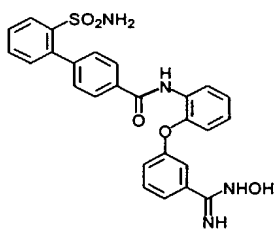
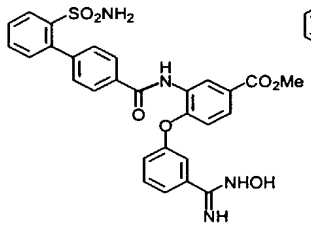
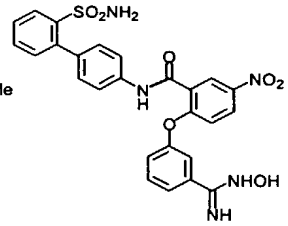
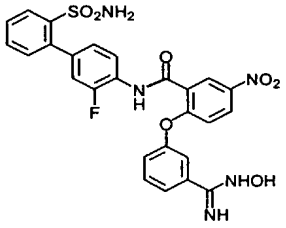
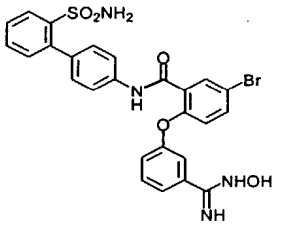


and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.

22. The compound according to claim 1 selected from the group consisting of: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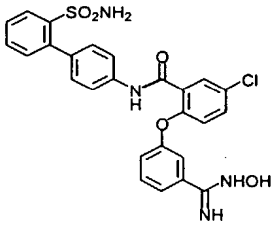
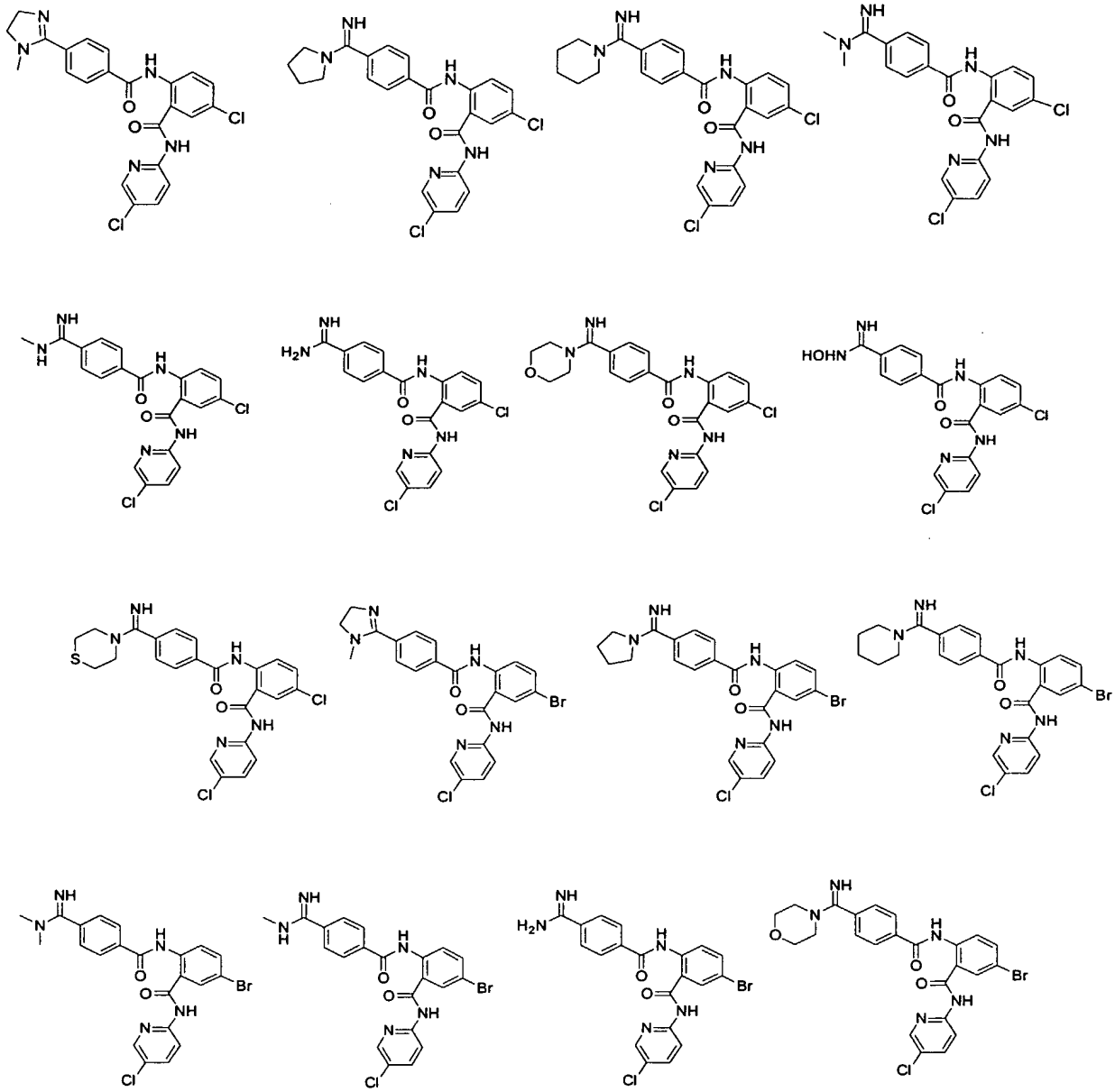
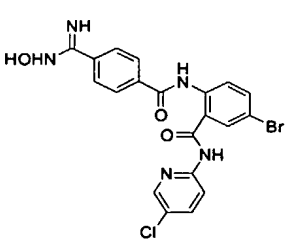
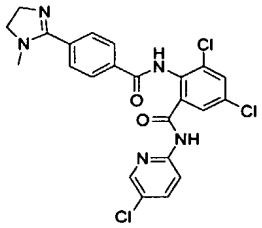
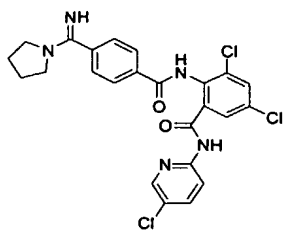
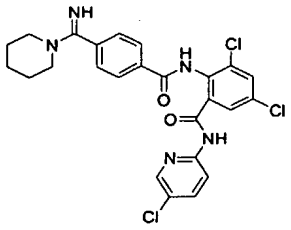
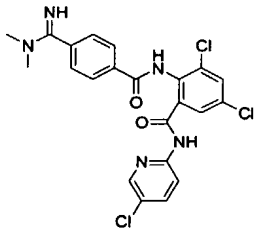
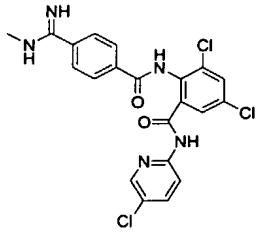
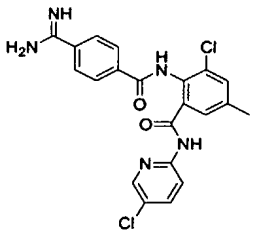
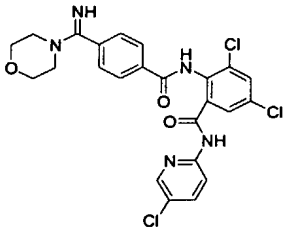


and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.

23. The compound according to claim 1 selected from the group consisting of:



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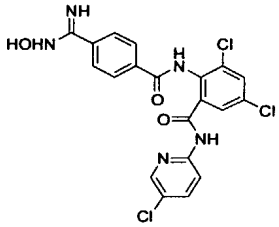
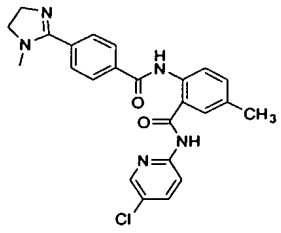
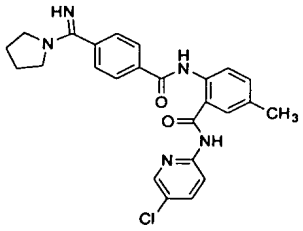
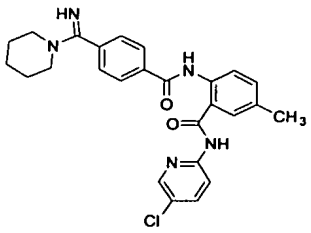
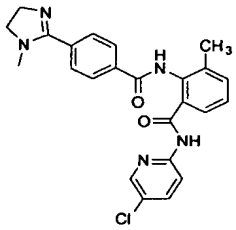
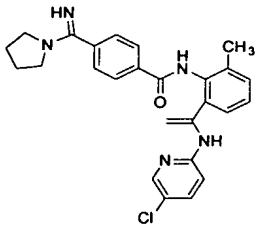


and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.

24. The compound according to claim 1 selected from the group consisting of: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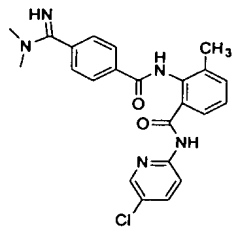
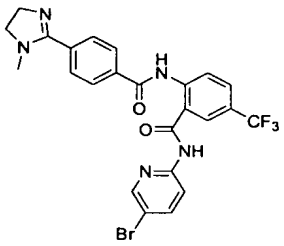
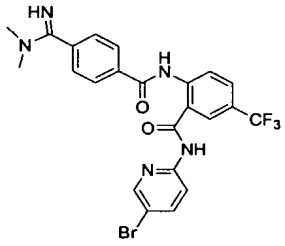
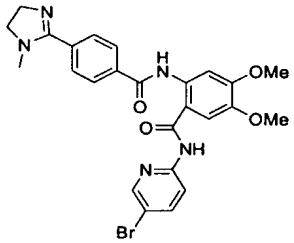


and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.

25. The compound according to claim 1 selected from the group consisting of: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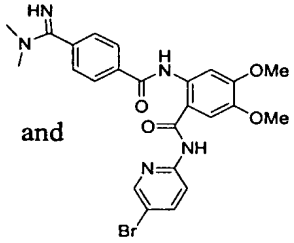
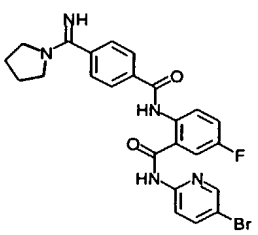
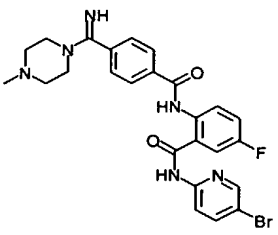
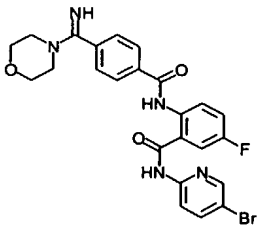
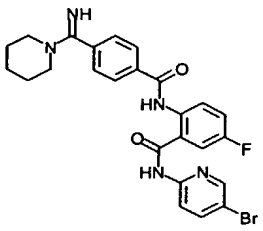
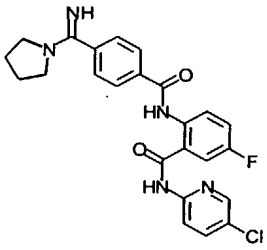
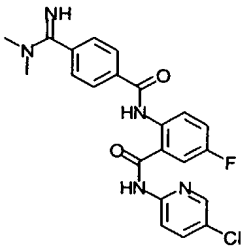
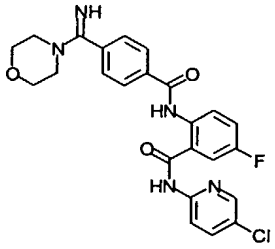
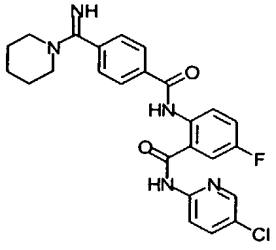
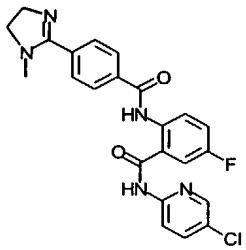
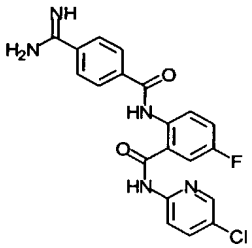
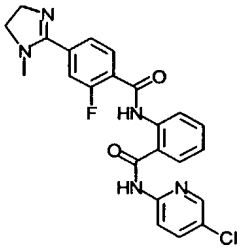
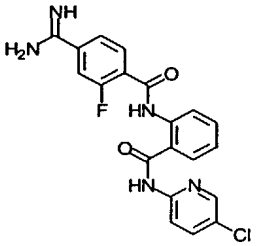
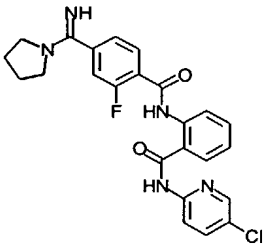
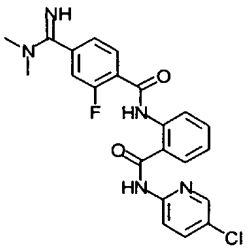
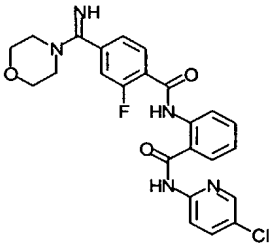
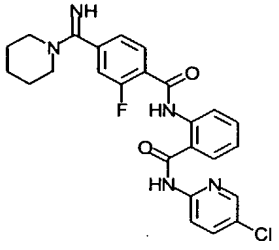
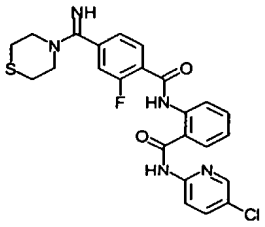
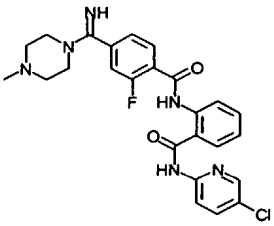
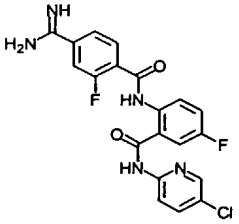
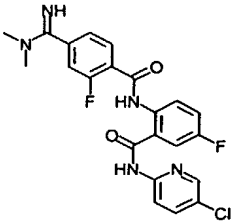
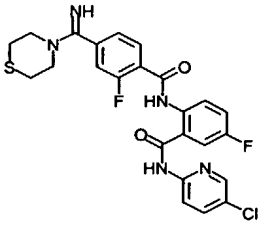
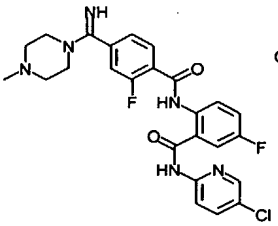
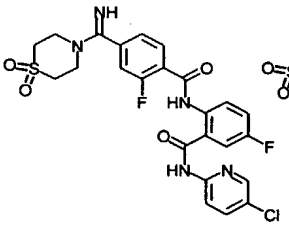
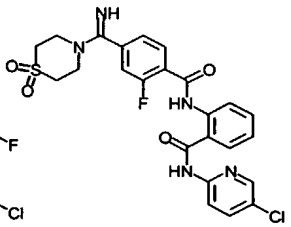
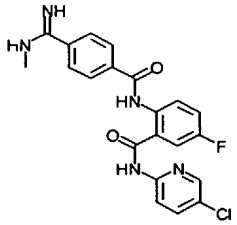
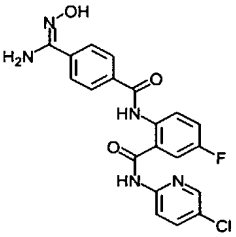
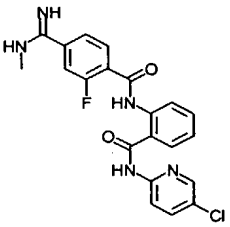
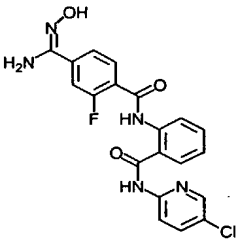
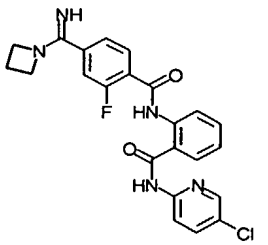
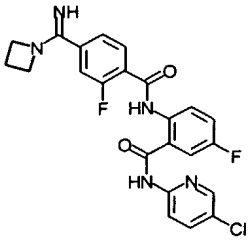
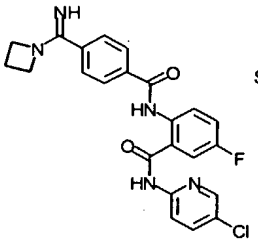
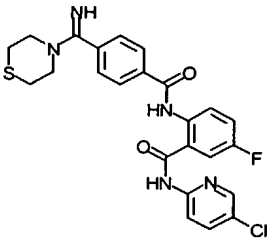
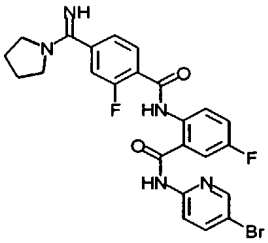
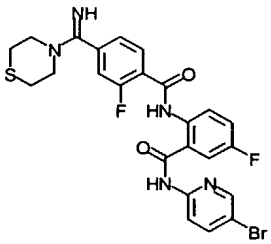
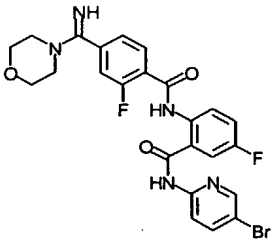
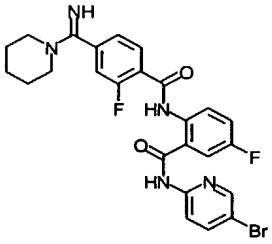
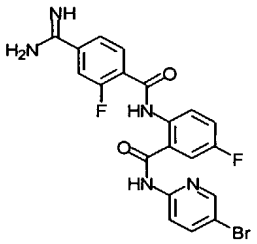
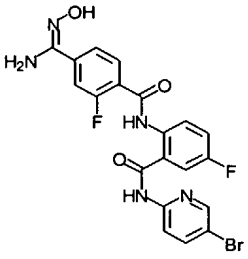
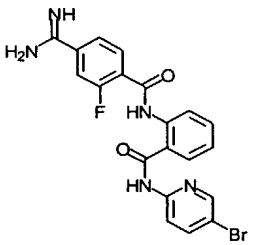
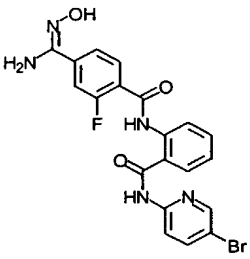


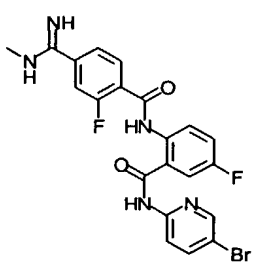
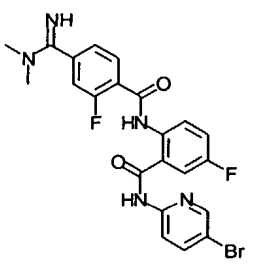
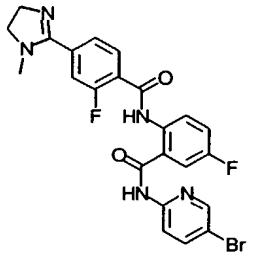
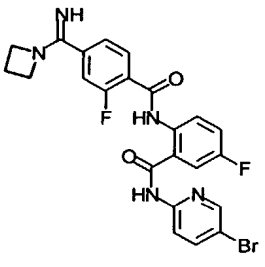
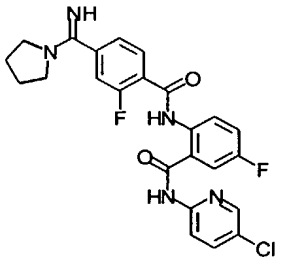
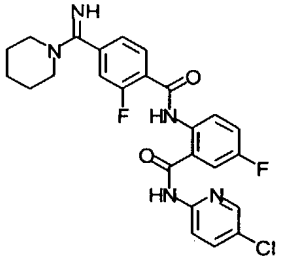
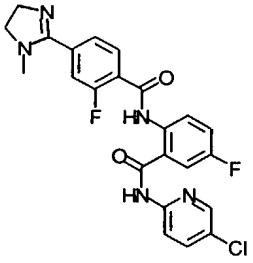
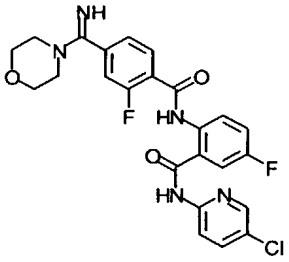
and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.

26. The compound according to claim 1, which is a member selected from the group consisting of:

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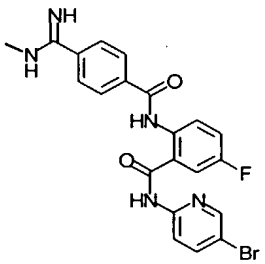
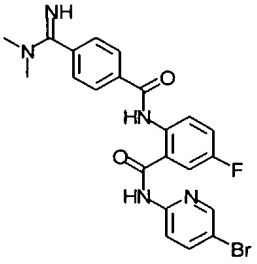
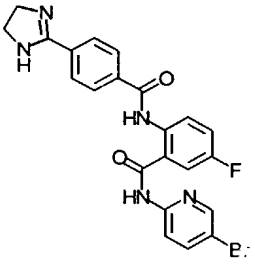
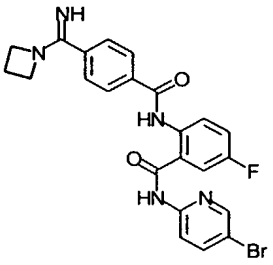

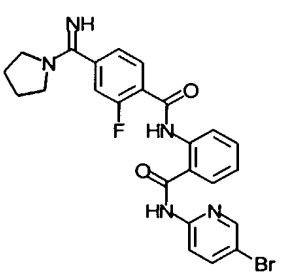
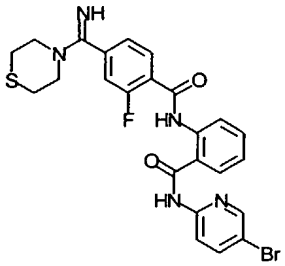
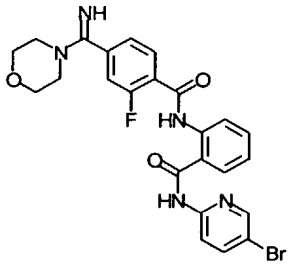
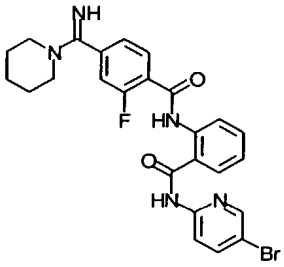

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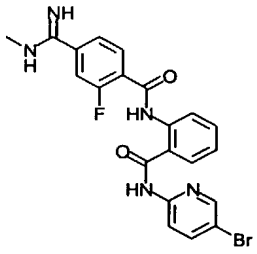
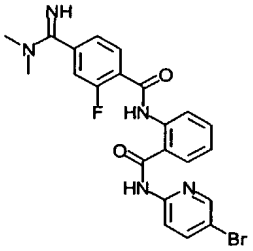
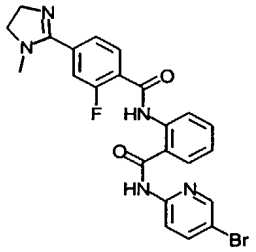
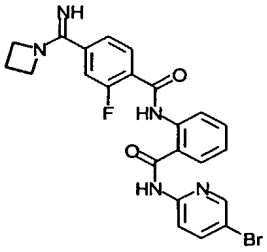

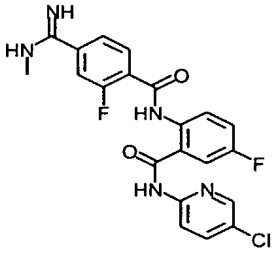

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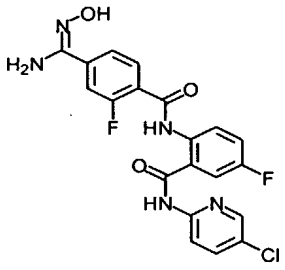

and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug
10 derivatives thereof.

27. A pharmaceutical composition for preventing or treating a condition in a

28. A method for preventing or treating a condition in a mammal characterized by undesired thrombosis comprising administering to said mammal a therapeutically effective amount of a compound of claim 1.

29. The method of claim 28, wherein the condition is selected from the group consisting of:

acute coronary syndrome, myocardial infarction, unstable angina, refractory angina, occlusive coronary thrombus occurring post-thrombolytic therapy or post-coronary angioplasty, a thrombotically mediated cerebrovascular syndrome, embolic stroke, thrombotic stroke, transient ischemic attacks, venous thrombosis, deep venous thrombosis, pulmonary embolus, coagulopathy, disseminated intravascular coagulation, thrombotic thrombocytopenic purpura, thromboangiitis obliterans, thrombotic disease associated with heparin-induced thrombocytopenia, thrombotic complications associated with extracorporeal circulation, thrombotic complications associated with instrumentation, and thrombotic complications associated with the fitting of prosthetic devices.

30. A method for inhibiting the coagulation of biological samples, comprising the step of administering a compound of claim 1.

31. A pharmaceutical composition for preventing or treating a condition in a mammal characterized by undesired thrombosis comprising a pharmaceutically acceptable carrier and a pharmaceutically effective amount of a compound of claim 2.

32. A method for preventing or treating a condition in a mammal characterized by undesired thrombosis comprising administering to said mammal a therapeutically effective amount of a compound of claim 2.

33. The method of claim 32, wherein the condition is selected from the group consisting of:

acute coronary syndrome, myocardial infarction, unstable angina, refractory angina, occlusive coronary thrombus occurring post-thrombolytic therapy or post-coronary angioplasty, a thrombotically mediated cerebrovascular syndrome, embolic stroke, thrombotic stroke, transient ischemic attacks, venous thrombosis, deep venous thrombosis, pulmonary embolus, coagulopathy, disseminated intravascular coagulation, thrombotic thrombocytopenic purpura, thromboangiitis obliterans, thrombotic disease associated with heparin-induced thrombocytopenia, thrombotic complications associated with extracorporeal circulation, thrombotic complications associated with instrumentation, and thrombotic complications associated with the fitting of prosthetic devices.

34. A method for inhibiting the coagulation of biological samples, comprising the step of administering a compound of claim 2.

35. A pharmaceutical composition for preventing or treating a condition in a mammal characterized by undesired thrombosis comprising a pharmaceutically acceptable carrier and a pharmaceutically effective amount of a compound of claim 3.

36. A method for preventing or treating a condition in a mammal characterized by undesired thrombosis comprising administering to said mammal a therapeutically effective amount of a compound of claim 3.

37. The method of claim 36, wherein the condition is selected from the group

post-coronary angioplasty, a thrombotically mediated cerebrovascular syndrome, embolic stroke, thrombotic stroke, transient ischemic attacks, venous thrombosis, deep venous thrombosis, pulmonary embolus, coagulopathy, disseminated intravascular coagulation, thrombotic thrombocytopenic purpura, thromboangiitis obliterans, thrombotic disease associated with heparin-induced thrombocytopenia, thrombotic complications associated with extracorporeal circulation, thrombotic complications associated with instrumentation, and thrombotic complications associated with the fitting of prosthetic devices.

38. A method for inhibiting the coagulation of biological samples, comprising the step of administering a compound of claim 3.

39. A pharmaceutical composition for preventing or treating a condition in a mammal characterized by undesired thrombosis comprising a pharmaceutically acceptable carrier and a pharmaceutically effective amount of a compound of claim 4.

40. A method for preventing or treating a condition in a mammal characterized by undesired thrombosis comprising administering to said mammal a therapeutically effective amount of a compound of claim 4.

41. The method of claim 40, wherein the condition is selected from the group consisting of:

acute coronary syndrome, myocardial infarction, unstable angina, refractory angina, occlusive coronary thrombus occurring post-thrombolytic therapy or post-coronary angioplasty, a thrombotically mediated cerebrovascular

thrombocytopenic purpura, thromboangiitis obliterans, thrombotic disease associated with heparin-induced thrombocytopenia, thrombotic complications associated with extracorporeal circulation, thrombotic complications associated with instrumentation, and thrombotic complications associated with the fitting of prosthetic devices.

42. A method for inhibiting the coagulation of biological samples, comprising the step of administering a compound of claim 4.

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
22 March 2001 (22.03.2001)

PCT

(10) International Publication Number
WO 01/19788 A3

(51) International Patent Classification[7]: C07C 311/16, 311/46, 317/40, 317/44, C07D 213/75, 213/81, 213/82, 217/22, 333/38, 401/12, 409/12, 409/14, 417/12, A61K 31/18, 31/33, A61P 7/02

(21) International Application Number: PCT/US00/25196

(22) International Filing Date:
15 September 2000 (15.09.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/154,332	17 September 1999 (17.09.1999)	US
60/185,746	29 February 2000 (29.02.2000)	US

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(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

(88) Date of publication of the international search report:
9 August 2001

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 01/19788 A3

(54) Title: BENZAMIDES AND RELATED INHIBITORS OF FACTOR Xa

(57) Abstract: Compounds of the formula A - Q - D - E - G - J - X in which D is a direct link, a substituted or unsubstituted phenyl or naphthyl group or a heterocyclic ring system; X is a substituted or unsubstituted phenyl or naphthyl group or a heterocyclic system; and the other variables are as defined in the claims, their salts and compositions related thereto having activity against mammalian factor Xa are disclosed. The compounds are useful in vitro or in vivo for preventing or treating coagulation disorders.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 00/25196

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07C311/16 C07C311/46 C07C317/40 C07C317/44 C07D213/75
C07D213/81 C07D213/82 C07D217/22 C07D333/38 C07D401/12
C07D409/12 C07D409/14 C07D417/12 A61K31/18 A61K31/33

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07C C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
BEILSTEIN Data, WPI Data, EPO-Internal, PAJ, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 57934 A (DU PONT MERCK PHARMACEUTICAL) 23 December 1998 (1998-12-23) page 2 -page 8; examples; table 1 ---	1-3, 27-42
X	WO 98 06694 A (DU PONT MERCK PHARMACEUTICAL) 19 February 1998 (1998-02-19) page 2 -page 7; examples; table 1A ---	1-3, 27-42
A	WO 98 28282 A (DU PONT MERCK PHARMACEUTICAL) 2 July 1998 (1998-07-02) page 3 -page 9; examples; table 1 ---	1-42
A	WO 98 28269 A (DU PONT MERCK PHARMACEUTICAL) 2 July 1998 (1998-07-02) page 3 -page 9; examples; table 1A ---	1-42

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"P" document published prior to the international filing date but later than the priority date claimed

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
26 February 2001	12/03/2001

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	ENGLISH, R

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 00/25196

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61P7/02

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	J.D. YOUNG, ET AL.: "Interannular interactions in para-substituted diphenylmethane anion redicals" JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, vol. 94, no. 25, 13 December 1972 (1972-12-13), pages 8790-8794, XP002161109 American Chemical Society, Washington, DC, US ISSN: 0002-7863 compound 3b	1

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[X] Further documents are listed in the continuation of box C.

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
26 February 2001	

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	ENGLISH, R

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Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 00/25196

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
X	H. SUZUKI, ET AL.: "Selective reduction with lithium aluminium hydride / diphosphorus tetraiodide" CHEMISTRY LETTERS, no. 6, June 1983 (1983-06), pages 909-910, XP002161110 Chemical Society of Japan, Tokyo, JP ISSN: 0366-7022 table 1, entries 5,14 ---	1
X	US 2 095 619 A (W.C. STOESSER, ET AL.) 12 October 1937 (1937-10-12) examples 1-6 ---	1
X	S. GOLDSCHMIDT, ET AL.: "Biphenyl derivatives II. Basic 4-biphenyl compounds" RECUEIL DES TRAVAUX CHIMIQUES DES PAYS-BAS., vol. 69, no. 9/10, September 1950 (1950-09), pages 1109-1117, XP002161111 Elsevier Science Publishers, Amsterdam, NL ISSN: 0165-0513 table I ---	1
X	W.F. COCKBURN, ET AL.: "Molecular rearrangement of tertiary amines. Part I" JOURNAL OF THE CHEMICAL SOCIETY, no. 8, August 1960 (1960-08), pages 3340-3346, XP002161112 Royal Society of Chemistry, Letchworth, GB page 3343, line 4 - line 5 -----	1

1

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1-3 (in part)

The initial phase of the search revealed a very large number of documents relevant to the issue of novelty. So many documents were retrieved that it is impossible to determine which part(s) of the claim(s) may be said to define subject-matter for which protection might legitimately be sought (Article 6 PCT).

For these reasons it appears impossible to execute a meaningful search and /or to issue a complete search report over the whole breadth of the claim(s). The search and the report for those claims can only be considered complete for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the compounds as indicated in the relevent examples (1-287) and claims 4-26.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 00/25196

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9857934 A	23-12-1998	AU 7976998 A	04-01-1999
		EP 0993448 A	19-04-2000
WO 9806694 A	19-02-1998	AU 4064597 A	06-03-1998
		EP 0934265 A	11-08-1999
		JP 2000516234 T	05-12-2000
		US 6057342 A	02-05-2000
WO 9828282 A	02-07-1998	AU 6645998 A	17-07-1998
		EP 0946528 A	06-10-1999
WO 9828269 A	02-07-1998	AU 5602098 A	17-07-1998
		CN 1246847 A	08-03-2000
		EP 0946508 A	06-10-1999
		HR 970698 A	31-10-1998
		LT 99076 A,B	25-02-2000
		LV 12430 A	20-02-2000
		LV 12430 B	20-07-2000
		NO 992633 A	20-08-1999
		PL 334250 A	14-02-2000
		SI 20017 A	29-02-2000
		US 6020357 A	01-02-2000
		BR 9714073 A	09-05-2000
US 2095619 A		NONE	